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Stereoselective Synthesis of β-Phenylselenoglycosides from Glycals and Rationalization of the Selenoglycosylation Processes

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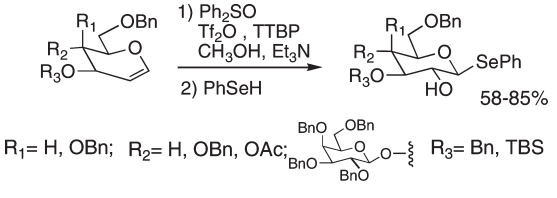
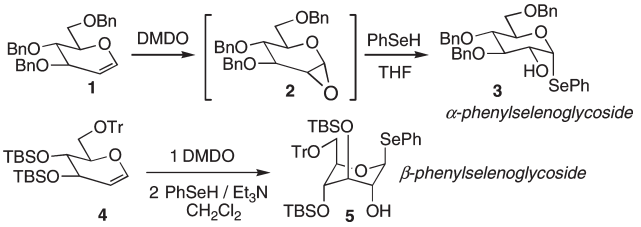


β-Phenylselenoglycosides have been efficiently and stereoselectively synthesized by direct oxidative glycosylation of benzenselenolate ($PhSe^-$) with glycals. A rationalization of the presently described β-selectivity and the opposite α-selectivity reported by Danishefsky in the ring-opening of epoxy glycals with benzeneselenol (PhSeH) is proposed.

In the past few years, considerable attention has been focused on selenoglycosides as useful and stable glycosyl donors for the preparation of oligosaccharides, *C*-glycosides, and glycoconjugates.[1] They are also interesting when used in an iterative glycosylation process for the construction of oligosaccharide libraries,[2] and for the preparation of C(2)-functionalized glycals.[3] Presently,[4] the most common synthetic routes to selenoglycosides involve the treatment of orthoester[5a] or 1-*O*-acetyl sugars[5b,c] with phenylselenol, treatment of glycosyl halides with diphenyl diselenide under reduction conditions,[6] or in a convenient odorless methodology with selenides derived from a zinc-dust/$ZnCl_2$ or indium(I) iodide-mediated cleavage of diselenide.[7] In a recent procedure used for the stereospecific synthesis of α- and β-selelenoglycosides and selenodisaccharides, *p*-methylbenzoyl selenoglycosides as the glycosyl donors are coupled with various electrophiles.[8] Moreover, only α-phenylselenoglycosides such as **3** can be efficiently synthesized starting from 3,4,6-*tri*-*O*-benzyl-D-glucal (**1**), via 1,2-anhydro derivative **2**, as reported by Danishefsky (Scheme 1).[9−11] Actually, in a single exception reported by Shuto,[12] β-phenylselenoglycoside **5** is obtained, via corresponding epoxide, from 3,4-di-*O*-*tert*-butyldimethylsilyl-6-*O*-trityl-D-glucal (**4**), but the β-stereoselective reaction is not generalized and seems to be limited only to this conformationally restricted substrate (Scheme 1). To date there have been no more reports of the synthesis of β-selenoglycosides starting from glycals.

SCHEME 1. α- and β-Phenylselenoglycosides from Glycals



(1) (a) Mehta, S.; Pinto, B. M. *J. Org. Chem.* **1993**, *58*, 3269. (b) Randell, K. D.; Johnston, B. D.; Brown, P. N.; Pinto, B. M. *Carbohydr. Res.* **2000**, *325*, 253. (c) Jiaang, W.-T.; Chang, M.-Y.; Tseng, P.-H.; Chen, S.-T. *Tetrahedron Lett.* **2000**, *41*, 3127. (d) Grant, L.; Liu, Y.; Walsh, K. E.; Walter, D. S.; Gallagher, T. *Org. Lett.* **2002**, *4*, 4623. (e) Mallet, A.; Mallet, J.-M.; Sinay, P. *Tetrahedron: Asymmetry* **1994**, *5*, 2593. (f) van Well, R. M.; Karkkainem, T. S.; Kartha, K. P. R.; Field, R. A. *Carbohydr. Res.* **2006**, *341*, 1391. (g) Valeria, S.; Iadonisi, A.; Adinolfi, M.; Ravidà, A. *J. Org. Chem.* **2007**, *72*, 6097. (h) For a comprehensive review on selenium-containing sugars see: Witczak, Z. J.; Czernecki, S. *Adv. Carbohydr. Chem. Biochem.* **1998**, *53*, 143.

(2) Yamago, S.; Yamada, T.; Ito, H.; Hara, O.; Mino, Y.; Yoshida, J.-i. *Chem.—Eur. J.* **2005**, *11*, 6159.

(3) Chambers, D. J.; Evans, G. R.; Fairbanks, A. J. *Tetrahedron* **2004**, *60*, 8411.

(4) For early synthetic approaches to selenoglycosides see: (a) Schneider, W.; Wrede, F. *Ber. Dtsch. Chem. Ges.* **1917**, *50*, 793. (b) Wrede, F. *Ber. Dtsch. Chem. Ges.* **1919**, *52*, 2153. (c) Bonner, W. A.; Robinson, A. *J. Am. Chem. Soc.* **1950**, *72*, 354.

(5) (a) Aloui, M.; Chambers, D. J.; Cumpstey, I.; Fairbanks, A. J.; Redgrave, A. J.; Seward, C. M. P. *Chem.—Eur. J.* **2002**, *8*, 2608. (b) Mehta, S.; Pinto, B. M. *Tetrahedron Lett.* **1991**, *32*, 4435. (c) Stork, G.; Suh, H. S.; Kim, G. *J. Am .Chem. Soc.* **1991**, *113*, 7054.

(6) Crich, D.; Suk, D.-H.; Sun, S. *Tetrahedron: Asymmetry* **2003**, *14*, 2861.

(7) (a) Mukherjee, C.; Tiwari, P.; Misra, A. K. *Tetrahedron Lett.* **2006**, *47*, 441. (b) Tiwari, P.; Misra, A. K. *Tetrahedron Lett.* **2006**, *47*, 2345.

(8) (a) Kawai, Y.; Ando, H.; Ozeki, H.; Koketsu, M.; Ishihara, H. *Org. Lett.* **2005**, *7*, 4653. (b) Nanami, M.; Ando, H.; Kawai, Y.; Koketsu, M.; Ishihara, H. *Tetrahedron Lett.* **2007**, *48*, 1113.

(9) (a) Gordon, D. M.; Danishefsky, S. J. *Carbohydr. Res.* **1990**, *206*, 361. In this procedure, contrary to the protocol originally employed with other nucleophiles, $ZnCl_2$ is not used as the promoting Lewis acid to open epoxide **2** synthetized with Murray's reagent DMDO (for DMDO preparation see: Murray, R.W.; Singh, M. *Org. Synth.* **1997**, *74*, 91). (b) Danishefsky, S. J.; Bilodeau, M. T. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1380.

(10) For pioneering studies on ring opening of 1,2-anhydropyranoside (Brigl anhydride) with benzeneselenol, see: Frenzel, H.; Nuhn, P.; Wagner, G. *Arch. Pharm.* **1962**, *302*, 62 and ref 1h.

(11) For electrophilic seleno activations of glycals see: (a) Jaurand, G.; Beau, J.-M.; Sinay, P. *J. Chem. Soc., Chem. Commun.* **1981**, 572. (b) Kaye, A.; Neidle, S.; Reese, C. B. *Tetrahedron Lett.* **1988**, *29*, 2711. (c) Santoyo-Gonzáles, F.; Calvo-Flores, F. G.; García-Mendoza, P.; Hernández-Mateo, F.; Isac-García, J.; Robles-Díaz, R. *J. Org. Chem.* **1993**, *58*, 6122. (d) Czernecki, S.; Ayadi, E.; Randriamandimby, D. *J. Org. Chem.* **1994**, *59*, 8256.

(12) (a) Shuto, S.; Terauchi, M.; Yahiro, Y.; Abe, H.; Ichikawa, S.; Matsuda, A. *Tetrahedron Lett.* **2000**, *41*, 4151. (b) Terauchi, M.; Yahiro, Y.; Abe, H.; Ichikawa, S.; Tovey, S. C.; Dedos, S. G.; Taylor, C. W.; Potter, B. V. L.; Matsuda, A.; Shuto, S. *Tetrahedron* **2005**, *61*, 3697 and references cited therein. Except for **5** and conformationally similar 3,4-di-*O*-TBDS- or 3,4-di-*O*-TIPS-D-glucal, other β-phenylselenoglycosides were prepared by the authors in a different way.

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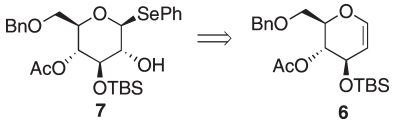
Furthermore, no rationalization was provided in order to justify the α-selectivity found by Danishefsky in the opening reaction of epoxide **2** by PhSeH, a result that differs from the usual β-selectivity obtained by the same author in the classic "glycal assembly" strategy with many other nucleophiles.[9b] The β-selectivity obtained by Shuto was not rationalized, either.

In this paper, we report a general protocol for the completely stereoselective synthesis of β-selenoglycosides starting from glycals, and we focus on the rationalization of the present results, as well as of previously reported data referring to the same matter.

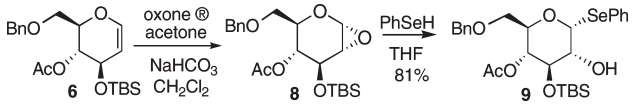
In the framework of studies dealing with the synthesis of new glycosyl donors, we needed β-phenylselenoglycoside **7**, bearing appropriate protecting groups on C(3), C(4), and C(6), as shown (Scheme 2). The use of glucal **6** as the precursor of **7** appeared to be particularly attractive for this purpose, provided that a 1,2-trans functionalization of the endocyclic π-system of **6** was possible (Scheme 2).

SCHEME 2. 1,2-Trans Functionalization of the Endocyclic π-System of Glucal 6



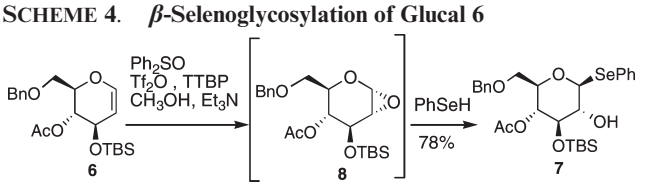
As expected, the nucleophilic addition of PhSeH, under Danishefsky's conditions,[9a] to a THF solution of 1,2-anhydropyranoside **8**, easily prepared from **6** by Dondoni's protocol,[13] afforded only the corresponding α-phenylselenoglycoside **9**, resulting from a completely stereoselective 1,2-cis functionalization of the π system of the starting glucal **6** (Scheme 3).

SCHEME 3. α-Selenoglycosylation of Glucal 6



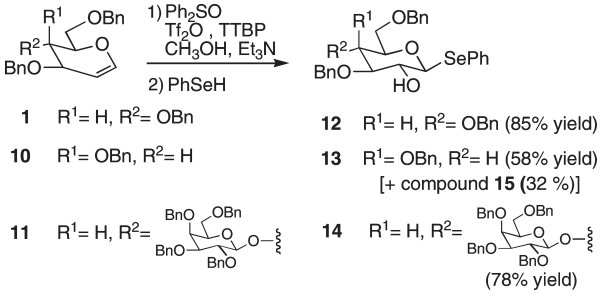
This result prompted us to verify whether a corresponding diastereoselective 1,2-trans functionalization of the π system of glucal **6** was feasible by a new application of Gin's direct oxidative glycosylation protocol[14] with PhSeH as the glycosyl acceptor. Much to our delight, as reported with most of the nucleophiles used in the original procedure, the desired 1,2-trans functionalization of **6** was obtained with a completely diastereoselective construction of the corresponding C(2)-α-hydroxy-β-phenylselenoglycoside **7**, needed for our synthetic purposes (Scheme 4).[15]

SCHEME 4. β-Selenoglycosylation of Glucal 6



An additional interest in this reaction derived from the observation that the β-selectivity obtained in the direct oxidative glycosidic coupling with PhSeH is not substrate dependent. In fact when other glycals such as glucal **1**, 3,4,6-tri-*O*-benzyl-D-galactal (**10**) and hexa-*O*-benzyl lactal (**11**)[16] are used, the corresponding β-phenylselenoglycosides **12**,[5a] **13**,[1e] and **14** are obtained, respectively, as the only glycosylation products (Scheme 5). It should be observed that in the glycosylation of PhSeH with galactal **10**, the formate derivative **15**, isomer of β- phenylselenoglycoside **13**, was also isolated (32%) as a byproduct of the reaction.

SCHEME 5. β-Selenoglycosylation of Glycals 1, 10, and 11



On the basis of the mechanism of Gin's direct oxidative glycosylation,[14b] a likely reaction pathway for the formation of formate **15** involves an initial α-approach[17] of the activated electrophilic diphenyl sulfoxide ($[Ph_2SOTf]^+[TfO]^-$) onto the C(2) position of galactal **10**, due to the steric hindrance to the usual β-approach[14b] by the C(4) axial substituent, to produce, with an excess of Ph_2SO, intermediate **16** (Scheme 6).

The subsequent addition of MeOH and Et_3N leads to the formation of β-epoxy galactal **17**, which in the presence of selenolate nucleophile allows the generation of α-selenoglycoside **18**. The diaxial disposition of the C(1) and C(2) substituents and the C(2)−OH activation by the $Ph_2SOMe^+TfO^-$ favors the intramolecular cyclization of **18** to α-episelenonium ion intermediate **19**. Final aqueous workup of **19** leads to the regioisomeric trans addition product **20**, which spontaneusly rearranges to formate **15**, as tentatively shown in Scheme 6.[18]

(13) Cheshev, P.; Marra, A.; Dondoni, A. *Carbohydr. Res.* **2006**, *341*, 2714.

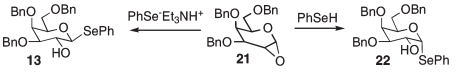
(14) (a) Di Bussolo, V.; Kim, Y.-J.; Gin, D. Y. *J. Am. Chem. Soc.* **1998**, *120*, 13515. (b) Honda, E.; Gin, D. Y. *J. Am. Chem. Soc.* **2002**, *124*, 7343.

(15) We found that when using PhSeH as the nucleophile in the direct oxidative glycosylation with glucal **6**, Lewis acid is not necessary for coupling to proceed.

(16) Upreti, M.; Ruhela, D.; Vishwakarma, R. A. *Tetrahedron* **2000**, *56*, 6577.

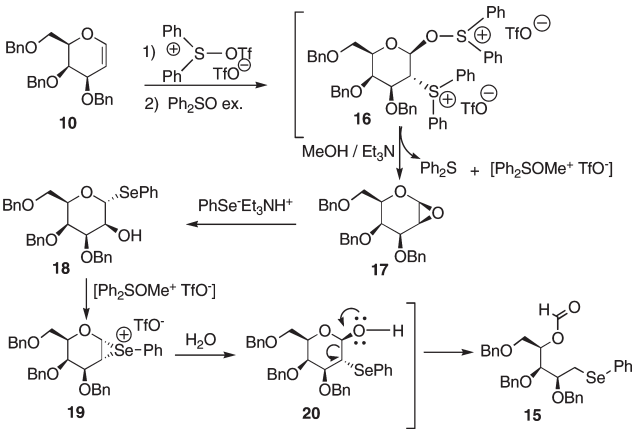
(17) For examples of α-approach of electrophilic reagents onto the C(2) position of protected glycals see: (a) Grewal, G.; Kaila, N.; Franck, R. W. *J. Org. Chem.* **1992**, *57*, 2084. (b) Roush, W. R.; Sebesta, D. P.; James, R. A. *Tetrahedron* **1997**, *53*, 8837.

(18) Traces (less than 5%) of the corresponding formate, inseparable from the glycosylation product, are also obtained in the β-phenylselenoglycosylation of glucal **6**. Control reaction carried out on β-phenylselenoglycoside **13** and α-phenylselenoglycoside **22**, independently synthetized by ring opening of epoxy galactal **21** (see ref 13) with PhSeH, showed the stability of both glycosides to the Gin's reaction conditions with no evident isomerization to formate **15**.



Investigations into the validity of the proposed reaction pathway proposed for the formation of **15** are currently underway.

SCHEME 6. Proposed Mechanism for the Formate 15

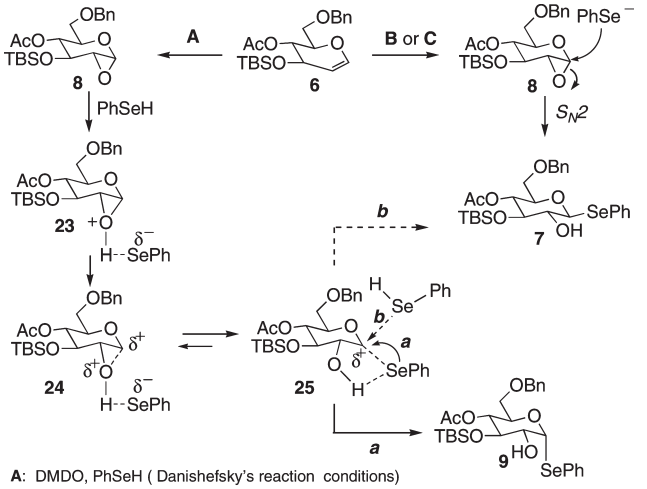


At this point an attractive challenge was to find an explanation for the different diastereoselective results observed in the glycosylation of PhSeH by means of two apparently very similar protocols: the α-selectivity observed in the oxirane ring-opening of epoxide **8** generated via DMDO oxidation of the corresponding glucal **6**, and the *β*-selectivity obtained by applying the direct oxidative glycosylation of PhSeH with glucal donor **6**. The following observations revealed some key aspects crucial for the formulation of an appropriate rationalization: (i) in both glycosylation procedures (Schemes 3 and 4), the glycosyl donor is an intermediate epoxide such as **8**, and the glycosyl acceptor (the nucleophile) is PhSeH; (ii) when glycosylation is carried out with the epoxide generated by DMDO oxidation, the reaction mixture is neutral, whereas it is somewhat alkaline when modified Gin's direct oxidative glycosylation is applied, due to the presence of an excess of Et_3N; and (iii) when PhSeH (pK_a = 5.9) is mixed with Et_3N following Gin's protocol, a complete, or almost complete, proton transfer occurs, with the formation of the triethylammonium selenolate salt (eq 1).[19]

$$PhSeH + Et_3N \rightleftharpoons PhSe^- Et_3NH^+ \qquad (1)$$

On this basis, we think that the above-described opposite stereoselective results simply depend on the different nature of the nucleophile present in the reaction mixture and involved in the ring-opening of the intermediate epoxide **8**. Under Danishefsky's conditions (Scheme 7, reaction conditions **A**), the nucleophile PhSeH is present in the undissociated form, which is acidic enough to protonate the oxirane oxygen and to determine the ring-opening of epoxide **8** under acid conditions, following the ion−dipole pair mechanism, as admitted in the case of 2-aryloxiranes.[20] In this way, the protonated epoxide **23** leads to an intramolecular intimate ion−dipole pair **24**, in which there is an extended oxirane oxygen−C(1) bond. By an internal rearrangement, **24** can evolve to the more carbocationic nucleophile-separated ion−dipole pair **25**.[21] Subsequent nucleophilic attack on C(1) of **25** would preferentially occur by the internal nucleophile, from the same side as the coordination, with complete retention of the configuration, to afford the *syn* adduct, the α-anomer **9** (*route* ***a***, Scheme 7), as experimentally found. In this framework the attack of the nucleophile internal to the ion−dipole pair **25** appears to be so entropically favored that a corresponding attack by an external nucleophile, which would lead to the corresponding *anti* adduct, the *β*-anomer **7** (*route* ***b***, Scheme 7), can reasonably be excluded.[22]

SCHEME 7. Rationalization of α- and *β*-Selenoglycosylation of Epoxide 8



On the other hand, when direct oxidative glycosylation is employed (Gin's protocol) (Scheme 7, reaction conditions **B**), the nucleophile (PhSeH) is mostly present, in the reaction mixture, in its corresponding deprotonated form ($PhSe^-$) due to the presence of an excess (4 equiv) of Et_3N. The phenylselenolate is such a strong nucleophile that it is able to open directly, in an S_N2-like fashion, the oxirane ring of **8**, with a complete inversion of configuration on C(1) affording the anti adduct, the *β* anomer **7**, as the only reaction product, through a completely *anti* stereoselective process.

To check the validity of the proposed rationalization, the ring-opening reaction of epoxy glucal **8**, obtained by oxidation of glucal **6** with in situ generated DMDO,[13] was performed with $PhSe^-Et_3NH^+$, independently prepared by reaction of PhSeH (3 equiv) and Et_3N (4 equiv) (Scheme 7, reaction conditions **C**). In these conditions, the nucleophile actually present in the reaction mixture ($PhSe^-$) cannot obviously "protonate" the oxirane oxygen of **8** and generate the intermediate species **25** (Scheme 7): it can only attack directly epoxide **8** in an S_N2-like process, affording the corresponding *anti* adduct, the *β*-phenylselenoglycoside **7**, as experimentally found.[23]

(19) Reich, H. J.; Cohen, M. L. *J. Org. Chem.* **1979**, *44*, 3148.

(20) (a) Crotti, P.; Di Bussolo, V.; Macchia, F.; Favero, L.; Pineschi, M.; Lucarelli, L.; Roselli, G.; Renzi, G. *J. Phys. Org. Chem.* **2005**, *18*, 321. (b) Crotti, P.; Dell'Omodarme, G.; Ferretti, M.; Macchia, F. *J. Am. Chem. Soc.* **1987**, *109*, 1463.

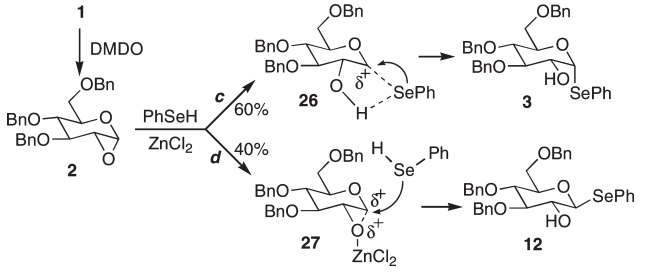
(21) The isomerization from the less carbocationic **24** to the more carbocationic intermediate **25** is favored by the ability of the endocyclic oxygen to stabilize, by conjugative electron-donating effect, the developing of an adjacent carbocationic center.

(22) For examples of cis opening of glycal epoxides metal-catalyzed see: (a) Rainier, J. D.; Cox, J. M. *Org. Lett.* **2000**, *2*, 2707. (b) Xue, S.; Han, K.-Z.; He, L.; Guo, Q.-X. *Synlett* **2003**, 870. (c) Wipf, P.; Pierce, J. G.; Zhuang, N. *Org. Lett.* **2005**, *7*, 483. (d) Sing, I.; Seitz, O. *Org. Lett.* **2006**, *8*, 4319. (e) Castilla, J.; Marín, I.; Matheu, M. I.; Díaz, Y.; Castillón, S. *J. Org. Chem.* **2010**, *75*, 514.

(23) The ring-opening reaction of epoxy galactal **21** (see ref 18) and epoxy glucal **2** with $PhSe^-Et_3NH^+$ also affords only *β*-selenoglycoside **13** and *β*-selenoglycoside **12**, respectively.

As further confirmation of our rationalization, when the ring-opening of epoxy glucal **2**, synthesized by DMDO oxidation of glucal **1**,[13] was carried out with PhSeH (3 equiv) in the presence of $ZnCl_2$ (2 equiv), a very significant 60:40 mixture of corresponding α-**3** and β-phenylselenoglycoside **12** was obtained (Scheme 8). Under these conditions, due to the contemporary presence of PhSeH and $ZnCl_2$, two different reaction pathways are reasonably possible. The coordination of PhSeH with the oxirane oxygen of **2** determines the occurrence of the ion−dipole pair mechanism which, through corresponding species **26**, leads to α-anomer **3** (*route c*, Scheme 8), whereas the competitive coordination of $ZnCl_2$ with **2** and subsequent formation of the corresponding species **27** necessarily leads to β-anomer **12** (*route d*, Scheme 8). Actually, in the coordinated species **27**, the C(1)−oxirane oxygen bond is not completely broken[24] and, as a consequence, the nucleophilic attack by PhSeH can occur only from the β-face, affording the *anti* adduct **12**. Analogously, when the same reaction was performed on epoxide **8** a corresponding 55:45 α-**9**/β-phenylselenoglycoside **7** mixture was obtained.[25]

SCHEME 8. Selenoglycosylation of Epoxide 2 whit PhSeH and $ZnCl_2$



In conclusion, the use of $PhSe^-$ (from PhSeH and Et_3N) allows a new synthetic access to β-phenylselenoglycosides from glycals. The completely opposite stereoselective results obtained in the glycosylation of PhSeH with glycals by Danishefsky's protocol (α-selenoglycosylation) and Gin's modified direct oxidative protocol (β-selenoglycosylation) are simply due to the nature of the nucleophile (PhSeH or $PhSe^-$) actually present in the reaction mixture. In our opinion, the different nucleophile determines a different ring-opening process (retention with PhSeH and inversion with $PhSe^-$) of the intermediate α-epoxy glycal and, as a consequence, the obtained opposite stereoselectivity. In this way, a completely stereodivergent selenoglycosylation process can be nicely obtained.

Experimental Section

Typical Procedure for β-Phenylselenoglycosylation of Glycals by Gin's Modified Direct Oxidative Protocol. Compound 7: Trifluoromethanesulfonic anhydride (0.48 mL, 2.88 mmol, 1.5 equiv) was added to a solution of diphenyl sulfoxide (1.165 g, 5.76 mmol, 3.0 equiv) and 2,4,6-tri-*tert*-butylpyridine (TTBP) (1.65 g, 6.72 mmol 3.5 equiv) in anhydrous CH_2Cl_2 (80 mL) at −78 °C. The reaction mixture was stirred at this temperature for 10 min then a solution of 4-*O*-acetyl-6-*O*-benzyl-3-*O*-(*tert*-butyldimethylsilyl)-D-glucal (**6**) (750 mg, 1.92 mmol, 1 equiv) in anhydrous CH_2Cl_2 (6 mL) was added and the mixture was stirred at this temperature for 30 min and then at −40 °C for 1 h. Methyl alcohol (78 μL, 1.92 mmol, 1 equiv) and triethylamine (1.02 mL, 7.68 mmol, 4 equiv) were added sequentially at −40 °C. The solution was stirred at this temperature for 30 min, at 0 °C for 2 h, then benzeneselenol (0.61 mL, 5.76 mmol, 3 equiv) was added. The mixture was stirred at 0 °C for 1 h and at 23 °C for 12 h. The reaction was diluted with CH_2Cl_2 (80 mL) and washed sequentially with sat aq $NaHCO_3$ (2 × 40 mL) and sat aq NaCl (40 mL). The organic layer was dried (Na_2SO_4) and concentrated, and the residue was purified by silica gel flash chromatography (10% EtOAc in hexane) to afford *phenyl 4-O-acetyl-6-O-benzyl-3-O-(tert-butyldimethylsilyl)-1-seleno-β-D-glucopyranoside* (**7**) as light yellow liquid (845 mg, 1.50 mmol, 78% yield): R_f (10% EtOAc in hexane) 0.25; $[\alpha]^{20}_D$ −17.1 (*c* 1.00, $CHCl_3$); IR (neat film) ν_{max} 3481, 2928, 1743, 1579, 1473, 1373, 1234, 1128 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.59−7.68 (m, 2H), 7.18−7.39 (m, 8H), 4.83 (t, 1H, *J* = 9.3 Hz), 4.74 (d, 1H, *J* = 10.3 Hz, H-1), 4.54 (d, 1H, *J* = 12.4 Hz), 4.49 (1H, *J* = 12.4 Hz), 3.65 (t, 1H, *J* = 8.7 Hz), 3.49−3.60 (m, 3H), 3.36 (ddd, 1H, *J* = 9.9, 8.5, and 2.5 Hz), 2.32 (d, 1H, *J* = 2.3 Hz), 1.96 (s, 3H), 0.84 (s, 9H), 0.10 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 170.1, 138.1, 135.1, 133.5, 129.4, 128.7, 128.1, 127.8, 127.1, 85.1, 79.1, 76.3, 73.7, 73.5, 72.3, 70.2, 25.8, 21.5, 18.3, −3.9, −4.8. Anal. Calcd for $C_{27}H_{38}O_6SeSi$: C, 57.33; H, 6.77. Found: C, 57.54; H, 6.49.

Typical Procedure for α-Phenylselenoglycosylation of Glycals by Danishefsky's Protocol. Compound 9: To a 0 °C vigorously stirred, biphasic solution of 4-*O*-acetyl-6-*O*-benzyl-3-*O*-(*tert*-butyldimethylsilyl)-D-glucal (**6**) (120 mg, 0.306 mmol, 1 equiv) in CH_2Cl_2 (1.5 mL), acetone (0.15 mL), and satd aq $NaHCO_3$ (2.5 mL) was added a solution of Oxone (377 mg, 0.612 mmol, 2 equiv) in H_2O (1.8 mL) dropwise over 10 min. The mixture was vigorously stirred at 0 °C for 30 min and then at rt for an additional 15 h. The reaction was diluted with CH_2Cl_2 and the organic phase was separated, dried (Na_2SO_3), and concentrated. The residue was immediatly dissolved in anhydrous THF (6 mL) and benzeneselenol (0.162 mL, 1.53 mmol, 5 equiv) was added. The mixture was stirred at 23 °C for 12 h then concentrated in vacuo. The residue was purified by silica gel flash chromatography (10% EtOAc in hexane) to afford *phenyl 4-O-acetyl-6-O-benzyl-3-O-(tert-butyldimethylsilyl)-1-seleno-α-D-glucopyranoside* (**9**) as light yellow liquid (140 mg, 0.25 mmol, 81%): R_f (10% EtOAc in hexane) 0.16; $[\alpha]^{20}_D$ +117.8 (*c* 1.31, $CHCl_3$); IR (neat film) ν_{max} 3475, 2918,1740, 1568, 1465, 1370, 1227, 1120 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.58−7.68 (m, 2H), 7.14−7.40 (m, 8H), 5.91 (d, 1H, *J* = 5.1 Hz, H-1), 4.98 (t, 1H, *J* = 5.1 Hz), 4.52 (d, 1H, *J* = 11.8 Hz), 4.45 (d, 1H, *J* = 11.8 Hz), 4.28−4.39 (m, 1H), 3.62−3.84 (m, 2H), 3.50−3.58 (m, 2H), 2.24 (d, 1H, *J* = 6.3 Hz), 2.00 (s, 3H), 0.88 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 169.8, 137.9, 134.5, 129.3, 128.9, 128.5, 128.1, 127.8, 89.6, 75.1, 73.6, 73.2, 72.3, 71.4, 69.3, 25.8, 21.4, 18.2, −4.0, −4.5. Anal. Calcd for $C_{27}H_{38}O_6SeSi$: C, 57.33; H, 6.77. Found: C, 57.59; H, 6.41.

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Supporting Information Available: Experimental procedures, full characterization data for new compounds, and copies of NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

(24) Anomeric selectivity in the opening of 1,2-anhydropyranosides with nucleophiles has been demostrated to be dependent on the nature of the Lewis acid and $ZnCl_2$ was found to be not able to determine the formation of a fully developed carbocationic species. See refs 9 and 14, as well as the following: Evans, D. A.; Trotter, B. W.; Côté, B. *Tetrahedron Lett.* **1998**, *39*, 1709.

(25) Control reactions carried out on phenylselenoglycosides **7** and **9** separately treated in THF solution with $ZnCl_2$ (2 equiv) did not lead to anomeric epimerization after 24 h at 23 °C.