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Azido-phenylselenylation of Protected Glycals

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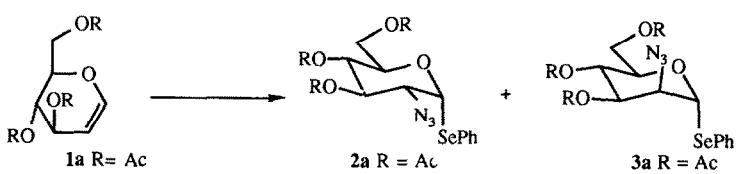
Abstract · *Anti-Markovnikov azido-phenylselenylation of diversely protected glycals affords protected phenyl 2-azido-2-deoxy-α-selenoglycopyranosides. From D-glucal, the α-manno and α-gluco isomers are obtained, whereas from D-galactal, a complete stereocontrol is observed, affording exclusively the α-galacto isomer in 70% yield*

Azido-phenylselenylation of double bonds is a very powerful and versatile reaction because it allows the one-step introduction of two functionalities in a molecule [1,2] 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 [1] Recently, Tingoli *et al.* obtained anti-Markovnikov addition products by treatment of an olefin with sodium azide and diphenyldiselenide in the presence of (diacetoxyiodo)benzene.[2] They proposed a mechanism initiated by addition to the olefin of an azido radical formed by oxidation of the azido ion. This study also includes the azido-phenylselenylation of 3,4-dihydro-2H-pyran Giuliano *et al.* reported the formation of mixtures of regioisomers in the azido-phenylselenylation of exocyclic alkenes under a variety of conditions.[3]

As a part of an ongoing programme directed towards the synthesis of selenoglycosides,[4] we expected that the radically induced azido-phenylselenylation of protected glycals would afford 2-azido-2-deoxy selenoglycosides which may function as precursors of 2-amino-2-deoxy selenoglycosides.

Commercially available tri-*O*-acetyl-**D**-glucal (**1a**) was employed to evaluate several oxidants and solvents in the presence of sodium azide and diphenyldiselenide



1a R= Ac
1b R= Bn

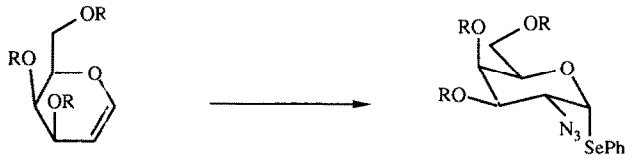
2a R = Ac
2b R = Bn

3a R = Ac
3b R = Bn

In agreement with the results of Tingoli *et al,* [2] the best results were obtained when **1a** (1 mmol) was reacted with (diacetoxyiodo)benzene (1.4 mmol) and sodium azide (2.4 mmol) in the presence of diphenyldiselenide (0.6 mmol) in CH_2Cl_2 (4 mL) at room temperature (48 h). After aqueous work-up and silica gel column chromatography (eluent: CH_2Cl_2) an inseparable mixture of **2a** and **3a** (6:4) was isolated in 88% yield.[5] The diastereomeric products were readily distinguished by examining the H-1 signals in the ^1H NMR

spectrum Interestingly, only the α-anomers were formed, as indicated by the values of the H-1, H-2 coupling constants (H-1 of the *gluco* isomer **2a**, δ 5 95 ppm, $J_{1,2}$= 5 3 Hz in $CDCl_3$, H-1 of the *manno* isomer **3a**, δ 5.8 ppm, broad s in $CDCl_3$)

When the benzylated **D**-glucal (**1b**) was reacted under the same conditions, a mixture of **2b** and **3b** was formed in the same ratio, however, degradation was observed before the reaction was complete [6] When **1b** was reacted with azidotrimethylsilane (4 eqt), tetra-n-butylammonium fluoride (0 2 eqt) and *N*-phenylselenophtalimide (*N*-PSP) (2 eqt) in methylene chloride as described by Giuliano *et al* for exocyclic alkenes, **2b** and **3b** (1:1) were obtained in 60% yield. This result is difficult to rationalize since no oxidant was present to generate the azido radical.



4a R = Ac
4b R = Bn

5a R = Ac
5b R = Bn

When tri-*O*-acetyl-**D**-galactal (**4a**) was treated with (diacetoxyiodo) benzene in the presence of $(PhSe)_2$ as for **1a**, the α-*galacto* isomer **5a** was obtained in crystalline form[5] (70%, mp 104-105°C, $[\alpha]_D$= +170° *c*=1 in CH_2Cl_2) The *galacto* configuration was unambiguously determined (H-1, δ 6.0 ppm, $J_{1,2}$= 5 4 Hz in $CDCl_3$) and no *talo* isomer[7] could be detected in the ^{1}H-NMR spectrum of the crude reaction mixture. When **4b** was reacted with *N*-PSP as for **1b**, the same diastereocontrol was observed and the α-*galacto* selenoglycoside **5b** was obtained as the sole product[5] (72%, oil, $[\alpha]_D$= +157° *c*=1 in CH_2Cl_2, H-1, δ 5 95 ppm, $J_{1,2}$= 5.22 Hz in $CDCl_3$).

Our results with the tri-*O*-acetyl-**D**-glycals are in good agreement with a rapid addition of electrophilic azido radical[8] to C-2 of the electron-rich double bond affording an anomeric radical stabilized in the α-configuration by the anomeric effect. Further homolytic reaction with $(PhSe)_2$ affords the α-selenoglycoside.[2] However more work is necessary to understand the mechanism of the reaction with *N*-PSP.

The easily obtained 2-azido-2-deoxy-selenoglycosides are versatile synthons which may be employed for a variety of transformations Their use as glycosyl donors is currently under investigation in our laboratory

References and Notes

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2 Tingoli, M.; Tiecco, M.; Chianelli, D.; Balducci, R , Temperini, A. *J Org Chem* **1991**, *56*, 6809-6813.
3 Giuliano, R. M , Duarte. F. *Synlett* **1992**, 419-421.
4. Benhaddou, R.; Czerneckı, S ; Randriamandimby, D *Synlett* **1992**, 967-968
5 All new compounds described gave C, H, N analysis and spectroscopic data in agreement with the structure. Selected data are given in the text
6 Presumably by oxidative cleavage of the benzyl groups. A mixture of **2b** and **3b** was isolated in 14% yield by working-up the reaction before important degradation.
2b-3b· ^{1}H-NMR ($CDCl_3$). δ, 3.5-4 4 (5H, m, H-3, H-4, H-5, H-6, H-6'), 4 4-5.0 (7H, m, 3 x CH_2 Benzyl, H-2), 5.8 (0.5H, bs, H-1 Manno), 5.9 (0 5H, d, $J_{1,2}$=4.9 Hz, H-1 Gluco), 7 0-7.5- (20H, m, Aromatic).
7. The *talo* azidonitrate is formed (4-8%) during azidonitration of diversely protected **D**-galactal derivatives Lemieux, R. U., Ratcliffe, R. M *Can J Chem* **1979**, *57*, 1244-1251 and, more recently, Marra, A , Gauffeny, F , Sinay, P *Tetrahedron* **1991**, *47*, 5149-5160
8 Minisci, F , Galli, R *Tetrahedron Lett* **1962**, *12*, 533-538

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