Substituted Azides from Selenium-promoted Deselenenylation of Azido Selenides. Glycosylation Reactions of Protected 2-Azido-2-deoxy-1-selenoglycopyranoses

Marco Tingoli,* Marcello Tiecco, Lorenzo Testaferri and Andrea Temperini

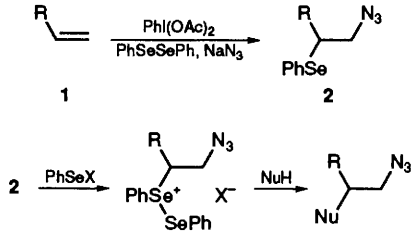
Istituto di Chimica Organica, Facoltà di Farmacia, Università di Perugia, Italy

After activation with electrophilic selenenylating agents, the phenylseleno group of vicinal azido selenides can be easily substituted by nucleophiles to afford a variety of substituted azides.

We have recently described the azido-phenylselenenylation of alkenes to produce compounds of type **2**.[1] These compounds are proving to be versatile intermediates for a range of inter- and intra-molecular reactions.[2–4]

Herein we describe a novel extension of these synthetic manipulations whereby the phenylselenenyl group may be displaced with another nucleophile whilst leaving the azido group intact (Scheme 1).

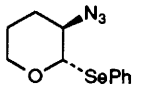
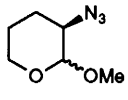
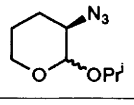
After treatment with electrophilic selenenylating agents, the vicinal azido selenides **2** can easily give rise to nucleophilic substitution reactions to afford a variety of substituted azides **4**. As indicated in Scheme 1, very likely the attack of the electrophilic selenenylating agents on the selenium atom of the selenides **2** generates the selenonium ion **3** in which the diphenyl diselenide acts as a very good leaving group.[5] The reaction was simply carried out by stirring, under nitrogen, the solution in the appropriate solvent of the seleno azide **2** (1 mmol) and of phenylselenenyl chloride, bromide or triflate[6] (1.1 mmol) for a few hours. The solvent was evaporated and the reaction products **4** were separated from the diphenyl diselenide by column chromatography on silica gel.† Experiments were carried out on the seleno azides derived from styrene, oct-1-ene and 3,4-dihydro-2*H*-pyran. Reaction conditions and yields are collected in Table 1. It can be observed that vicinal chloro-, bromo-, acetamido-, acetoxy- and alkoxy-azides are obtained in good yields in every case.‡



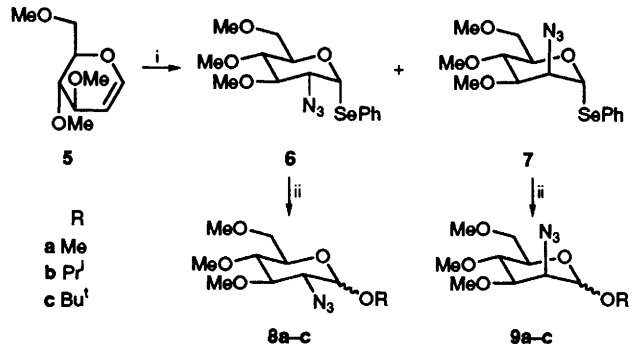
Scheme 1

It is likely the above described selenium promoted deselenenylation of the seleno azides **2** can also be applied to other phenyl alkyl selenides and that other nucleophiles can be employed. Thus, this method can probably find a much wider application. As a matter of fact we have used this selenium induced deselenenylation process to effect *O*-glycosylation reactions under extremely mild reaction conditions. Very recently our procedure of radical azido selenenylation of

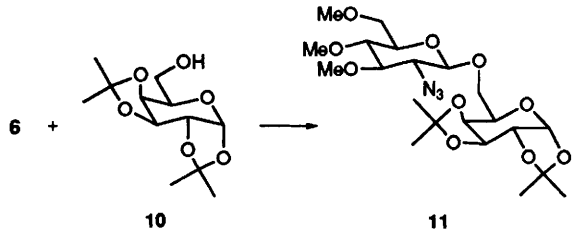
Table 1 Conversion of seleno azides **2** into substituted azides **4** promoted by electrophilic selenenylating agents[a]

	Seleno azide **2**	PhSeX	Solvent	*t*/h	Substituted azide **4**	Yield (%)[b]
a	$PhCHCH_2N_3$ | SePh	PhSeCl	MeCN	5	$PhCHCH_2N_3$ | Cl	95
b		PhSeBr	MeCN	2	$PhCHCH_2N_3$ | Br	67
c		PhSeOTf	MeCN–H_2O (4:1)	5	$PhCHCH_2N_3$ | NHCOMe	90
d		PhSeOTf	$MeCO_2H$	1	$PhCHCH_2N_3$ | OCOMe	75
e		PhSeOTf	MeOH	5	$PhCHCH_2N_3$ | OMe	87
f	$C_6H_{13}CHCH_2N_3$ | SePh	PhSeCl	MeCN	9	$C_6H_{13}CHCH_2N_3$ | Cl	65
g		PhSeBr	MeCN	8	$C_6H_{13}CHCH_2N_3$ | Br	50
h		PhSeOTf	MeOH	3		82[c]
i		PhSeOTf	MeCN–Pr^iOH (4:1)	3		70[d]

[a] The starting products were prepared according to the previously described general procedure.[1] The reactions with PhSeCl or PhSeBr were carried out at 80 °C and those with PhSeOTf at room temp. [b] Calculated from isolated products after column chromatography. [c] 3:1 Mixture of two stereoisomers. [d] 1:1 Mixture of two stereoisomers separated by column chromatography.



Scheme 2 *Reagents and conditions*: i, $PhI(OAc)_2$, PhSeSePh, NaN_3, CH_2Cl_2, room temp.; ii, PhSeOTf, MeCN, ROH, room temp.



Scheme 3

alkenes was applied to protected glycals in order to produce phenyl 2-azido-2-deoxy-1-selenoglycosides as efficient 2-azido-2-deoxyglycosyl donors.[7–9] For this purpose these compounds were hydrolysed with mercury(II) trifluoroacetate.[9] Furthermore, it has been recently reported that phenyl selenoglycosides can also behave as versatile glycosyl acceptors in glycosylation reactions.[10] The azido selenenylation of the tri-*O*-methyl-D-glycal **5**, easily obtained from the commercially available tri-*O*-acetyl-D-glycal, afforded a mixture (40:60) of **6** and **7** in 72% yield. The two isomers could be easily separated by column chromatography.§ In agreement with previous observations[7–9] only the α-anomers were obtained (Scheme 2).

The seleno azides **6** and **7** were subjected to selenium promoted deselenenylation reactions using PhSeOTf and different alcohols. The reaction of **6** in methanol afforded only the β-isomer **8a** in 93% yield.¶ The same reaction carried out in Pr^iOH–MeCN (1:4) gave **8b** in 73% yield as a 4:1 mixture of the β- and α-anomers which could not be separated. Similarly, a 76% yield of a 7:3 mixture of the β- and α-anomers **8c** was obtained from the reaction of **6** in Bu^tOH–MeCN (1:4). Under the same conditions reactions of **7** gave the methyl **9a** (92%, β:α = 3:2), *iso*-propyl **9b** (70%, β:α = 3:7) and *tert*-butyl **9c** (74%, β:α = 1:4) derivatives. In this case the two isomers were separated by column chromatography. Finally, the *gluco* isomer **6** was deselenenylated with PhSeOTf in MeCN in the presence of the 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose **10** (Scheme 3). In this case also the deselenenylation proceeded smoothly and afforded, as the sole reaction product in 60% yield, the 1,2:3,4-di-*O*-isopropylidene-6-*O*-[3,4,6-tri-*O*-methyl-2-deoxy-2-azido-β-D-glucopyranosyl]-α-D-galactopyranose **11**. Phenylselenenyl triflate has been recently employed to effect similar glycosylation reactions using thioglycosides.[11–13] The present procedure complements and improves the methods available to effect this important type of reaction.

Financial support from the CNR, Rome, and Ministero dell'Università e della Ricerca Scientifica e Tecnologica, Italy, is gratefully acknowledged.

Received, 11th April 1994; Com. 4/02123A

Footnotes

† When PhSeOTf was employed the reaction mixtures were filtered before evaporation of the solvent.

‡ The reaction products were fully characterized by ^1H, ^{13}C NMR and IR spectra and by GC-MS.

§ In previous work[7–9] the acetyl or benzyl derivatives were employed and the two isomeric reaction products could not be separated. Structural assignments were easily made by proton NMR spectroscopy. In $CDCl_3$, the H-1 atom of the *gluco* isomer **6** at δ 5.83 shows $J_{1,2}$ = 5.3 Hz, whereas the H-1 atom of the *manno* isomer **7** at δ 5.78 shows $J_{1,2}$ = 1.5 Hz).

¶ The course of this reaction was influenced by the solvent. In MeOH–MeCN or in MeOH–CH_2Cl_2 (1:4) mixtures the β- and α-anomers were obtained in 76 or 74% yield and in 95:5 or 65:35 ratio respectively.

References

1 M. Tingoli, M. Tiecco, D. Chianelli, R. Balducci and A. Temperini, *J. Org. Chem.*, 1991, **56**, 6809.
2 P. Molina, M. J. Vilaplana and A. Pastor, *Synthesis*, 1992, 873 and references cited therein.
3 M. Tingoli, M. Tiecco, L. Testaferri, R. Balducci and R. Andrenacci, *J. Org. Chem.*, 1993, **58**, 6097.
4 C. Paulmier, *Selenium Reagents and Intermediates in Organic Synthesis*, Pergamon, Oxford, 1986; D. Liotta, *Organoselenium Chemistry*, Wiley Interscience, New York, 1987.
5 M. Tiecco, L. Testaferri, M. Tingoli, D. Chianelli and D. Bartoli, *Tetrahedron*, 1988, **44**, 2261.
6 S. Murata and T. Suzuki, *Chem. Lett.*, 1987, 849.
7 F. Santoyo-González, F. G. Calvo-Flores, P. García-Mendoza, F. Hernández-Mateo, J. Isac-García and R. Robles-Díaz, *J. Org. Chem.*, 1993, **58**, 6122.
8 S. Czernecki and D. Randriamandimby, *Tetrahedron Lett.*, 1993, **34**, 7915.
9 S. Czernecki, E. Ayadi and D. Randriamandimby, *J. Chem. Soc., Chem. Commun.*, 1994, 35.
10 S. Mehta and B. M. Pinto, *J. Org. Chem.*, 1993, **58**, 3269.
11 Y. Matsuzaki, S. Nunomura, Y. Ito, M. Sugimoto, Y. Nakahara and T. Ogawa. *Carbohydr. Res.*, 1993, **242**, C1.
12 Y. Ito, T. Ogawa, M. Numata and M. Sugimoto, *Carbohydr. Res.*, 1990, **202**, 165.
13 Y. Ito and T. Ogawa, *Tetrahedron Lett.*, 1988, **29**, 1061.