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An Improved Phenylselenoetherification of Pent-4-en-1-ol

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Summary. The procedure employs phenylselenyl chloride or bromide, pent-4-en-1-ol, and additives, like pyridine and silver(I) salts, to generate the cyclic ether of tetrahydrofuran type in high yields. A catalytic amount of additive leads to higher yields, but equimolar amounts achieved almost quantitative yields under extremely mild experimental conditions. The effect of the halide ion of the selenylating reagent is not significant.

Keywords. Additive; Alcohol; Cyclization; Phenylselenoetherification; Furan.

Introduction

During the last years, cyclic ethers have attracted considerable attention due to their occurrence in several groups of natural compounds exhibiting important biological activities [1]. These units can be found in monocyclic or polycyclic compounds, fused with other cyclic ethers or forming spiro systems [2]. The presence of molecules with oxygenated heterocycles in nature is receiving considerable attention considering their capacity of modification of the transport of the Na^+, K^+, and Ca^{2+} cations through lipid membranes [3–6]. This activity is responsible for their antibiotic [3], neurotoxic [7, 8], antiviral [9], and cytotoxic action [10, 11], and as growth regulators [3, 12, 13] or inhibitors of the level of cholesterol in blood [14].

A number of synthesis approaches have been devised in order to construct the cyclic ether moiety using a carbon–carbon [15–22] or a carbon–oxygen [23–34] cyclization step, or modifying a cyclic precursor [35–41].

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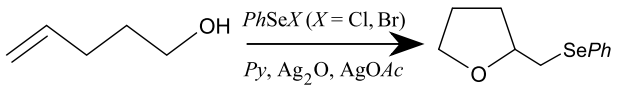
Results and Discussion

In recent years, we have studied the intramolecular cyclization of some Δ^4- and Δ^5-alkenols by means of benzeneselenyl halides *Ph*Se*X* ($X = $ Cl, Br) [29, 40–42]. Intramolecular heterocyclization is the main reaction in the case of all investigated primary and secondary alkenols, while tertiary alkenols, under the same experimental conditions are not converted into cyclic products at all by *Ph*SeBr and in a small amount by *Ph*SeCl. Although the addition products are expected, we have found that all investigated tertiary alkenols in the reaction with *Ph*SeBr [41] afforded γ- and δ-bromoalkanols in high yields (about 90%).

Recently [42], we have presented an approach to cyclic ethers from tertiary alkenols using *Ph*Se*X* ($X = $ Cl, Br) in the presence of pyridine. We found that the yields of the cyclic ethers are quantitative. In this paper, we present the extension of the methodology to pent-4-en-1-ol (**1**) and with Ag_2O and AgO*Ac* as additives. This alkenol yields the tetrahydrofuran ring, which is a commonly encountered substructure in many natural products showing interesting biological properties. The results of our investigation are shown in Table 1 and Scheme 1. These results show that all reactions proceeded to form oxygen heterocycles bearing the phenylseleno moiety in high yields (Table 1).

Table 1. Phenylselenoetherification of pent-4-en-1-ol without additive (a) and in the presence of a catalytic (A) and equimolar (B) amount of pyridine (b), Ag_2O (c), and AgO*Ac* (d)

alkenol	product		Yields of cyclic products/%							
			*Ph*SeCl				*Ph*SeBr			
1	**2**		a	b	c	d	a	b	c	d
		A	69	97	99	96	63	95	97	92
		B	69	100	97	92	63	100	95	90



1 **2**

Scheme 1

Cyclization is facilitated by the presence of pyridine, Ag_2O, and AgO*Ac*. Yields of products are higher and reaction time is shorter. Catalytic amounts of additives lead to higher yields, but an equimolar amount gives almost quantitative yields. As we can see from Table 1, pyridine shows the best results in the case of an equimolar amount, and Ag_2O is the best catalyst for this type of cyclization. The cyclization using a stoichometric amount of Ag_2O was completed faster than by using catalytic amounts only. It appears that the presence of pyridine is beneficial to the cyclization process due to its basic properties. All additives could enhance the nucleophilicity of the hydroxyl group of the alkenol and also mediate the stabilization of the oxonium ion intermediates. On the other hand, the reaction without a catalyst did not afford the desired product in practical yield. Also, the additive caused a dramatic increase in reaction rate. Thus, the reactions were completed in a few minutes (without additives the reaction time is half an hour to several hours).

This improved procedure for phenyselenoetherification should prove simpler and superior to those currently available. As for the yields of cyclic ethers, the procedure described gave better results than reported procedures. Accompanied by other merits, such as the mildness of the reaction conditions and the simplicity of the experimental procedure, our procedure is the most attractive one for the conversion of alkenols into oxacyclic compounds.

Experimental

Gas–liquid chromatography (GLC) analysis was performed with a Deni instrument, model 2000 with capillary apolar columns. ^1H and ^{13}C NMR spectra were run in $CDCl_3$ on a Varian Gemini 200 MHz NMR spectrometer. IR spectra were obtained with Perkin-Elmer Model 137B and Nicolet 7000 FT spectrophotometers. Thin-layer chromatography (TLC) was carried out on 0.25 mm E. Merck precoated silica gel plates (60F-254) using UV light for visualization. For column chromatography, E. Merck silica gel (60, particle size 0.063–0.200 mm) was used.

General Procedure

All reactions were carried out on a 1 mmol scale. To a magnetically stirred solution of alkenol **1** (1 mmol) and 0.1 mmol or 1 mmol additive in 5 cm^3 dry CH_2Cl_2 was added 0.212 g solid *Ph*SeCl (1.1 mmol) or 0.260 g *Ph*SeBr (1.1 mmol) at room temperature. The reaction went to completion within a few minutes. The pale yellow solution was washed (in the case of pyridine as an additive) with 5 cm^3 1 *M* HCl aqueous solution, saturated $NaHCO_3$, and then brine, or with saturated $NaHCO_3$ and H_2O (in the case of Ag_2O and AgO*Ac*). The organic layer was dried (Na_2SO_4), concentrated, and chromatography was performed. The product was obtained after elution of traces of diphenyl diselenide from a silica gel column using CH_2Cl_2. All the products were characterized and identified on the basis of their spectral data. The cyclic ether product **2** is a known compound. Its spectroscopic data has been given previously [29].

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