

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

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Summary. The procedure employs phenylselenenyl 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].

Results and Discussion

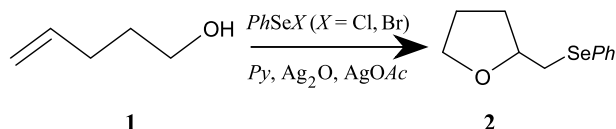
In recent years, we have studied the intramolecular cyclization of some Δ^4 - and Δ^5 -alkenols by means of benzeneselenenyl halides PhSeX ($\text{X} = \text{Cl}, \text{Br}$) [29, 40–42]. Intramolecular heterocyclization is the main reaction in the case of all investigated primary and secondary alkenols, while tertiary alkenols, under the same experimental conditions are not converted into cyclic products at all by PhSeBr and in a small amount by PhSeCl . Although the addition products are expected, we have found that all investigated tertiary alkenols in the reaction with PhSeBr [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 PhSeX ($\text{X} = \text{Cl}, \text{Br}$) 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 AgOAc 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).

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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), Ag₂O (c), and AgOAc (d)

alkenol	product	Yields of cyclic products/%							
		<i>PhSeCl</i>				<i>PhSeBr</i>			
		a	b	c	d	a	b	c	d
1	2								
	A	69	97	99	96	63	95	97	92
	B	69	100	97	92	63	100	95	90



Scheme 1

Cyclization is facilitated by the presence of pyridine, Ag₂O, and AgOAc. 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 Ag₂O is the best catalyst for this type of cyclization. The cyclization using a stoichiometric amount of Ag₂O 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 phenylselenoetherification 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 ¹³C NMR spectra were run in CDCl₃ 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 cm³ dry CH₂Cl₂ was added 0.212 g solid *PhSeCl* (1.1 mmol) or 0.260 g *PhSeBr* (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 cm³ 1 M HCl aqueous solution, saturated NaHCO₃, and then brine, or with saturated NaHCO₃ and H₂O (in the case of Ag₂O and AgOAc). The organic layer was dried (Na₂SO₄), concentrated, and chromatography was performed. The product was obtained after elution of traces of diphenyl diselenide from a silica gel column using CH₂Cl₂. 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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References

- [1] Yasumoto T, Murata M (1993) *Chem Rev* **93**: 1897
- [2] Faulkner D (1997) *J Nat Prod Rep* **14**: 259
- [3] Wesley JW (1982) *Polyether Antibiotics Naturally Occurring Acid Ionophores*, Marcel Dekker, New York, Vols I and II
- [4] Painter GR, Presman BC (1982) *Top Curr Chem* **101**: 83
- [5] Still WC, Hauck P, Kempf D (1987) *Tetrahedron Lett* **28**: 2817
- [6] Smith PW, Still WC (1988) *J Am Chem Soc* **110**: 7917
- [7] Shimizu Y, Marine Natural Products, Scheuer P (1978) Academic press, New York, Vol I, p 1
- [8] Ellis S (1985) *Toksikon* **23**: 469
- [9] Sakemi S, Higa T, Jefford CW, Bernardinelli G (1986) *Tetrahedron Lett* **27**: 4287
- [10] Suzuki T, Suzuki A, Furusaki T, Matsumoto A, Kato A, Imanaka Y, Kurosawa E (1985) *Tetrahedron Lett* **26**: 1329
- [11] Corley DG, Herb RR, Moore E, Scheuer PJ, Paul VJ (1988) *J Org Chem* **53**: 3644
- [12] Cohran VM (1958) *Physiology of Fungi*, Wiley, New York
- [13] Schreiber SL, Kelly SE, Porco JA, Sanmakia T, Suh EM (1988) *J Am Chem Soc* **110**: 6210

- [14] González AG, Martin JD, Martin VS, Norte M, Pérez R, Ruano JZ, Drexler SA, Clardy J (1982) *Tetrahedron* **38**: 1009
- [15] Ravelo JL, Regueiro A, Martin JD (1992) *Tetrahedron Lett* **33**: 3389
- [16] Hoffmann RW, Münster I (1995) *Tetrahedron Lett* **36**: 1431
- [17] Alvarez E, Diaz MT, Hanxing L, Martin JD (1995) *J Am Chem Soc* **117**: 1437
- [18] Clark JS, Kettle JG (1997) *Tetrahedron Lett* **38**: 127
- [19] Inoue M, Sasaki M, Tachibana K (1997) *Tetrahedron Lett* **38**: 1611
- [20] Berger D, Overman LE, Renhowe PA (1997) *J Am Chem Soc* **119**: 2446
- [21] Crimmins MT, Choy AL (1997) *J Org Chem* **62**: 7548
- [22] Nicolaou KC, Prasad CVC, Hwang CK, Duggan ME, Veale CA (1989) *J Am Chem Soc* **111**: 5321
- [23] Nicolaou KC, Prasad CVC, Somers PK, Hwang CK (1989) *J Am Chem Soc* **111**: 5330
- [24] Nicolaou KC, Prasad CVC, Somers PK, Hwang CK (1989) *J Am Chem Soc* **111**: 5335
- [25] Cooper AJ, Salomon RG (1990) *Tetrahedron Lett* **31**: 3813
- [26] Suzuki T, Sato O, Hiram M (1990) *Tetrahedron Lett* **31**: 4747
- [27] Aicher TD, Buszek KR, Fang FK, Forsyth CJ, Jung SH, Kishi Y, Scola PM (1992) *Tetrahedron Lett* **33**: 1549
- [28] Martin VS, Polazón JM (1992) *Tetrahedron Lett* **33**: 2399
- [29] Konstantinovic S, Bugarcic Z, Milosavljevic S, Schroth G, Mihailovic MLJ (1992) *Liebigs Ann Chem* **261**
- [30] Gung BW, Francis MB (1993) *J Org Chem* **58**: 6177
- [31] Mukai C, Ikeda Y, Sugimoto Y, Hanaoka M (1994) *Tetrahedron Lett* **35**: 2179
- [32] Mukai C, Sugimoto Y, Ikeda Y, Hanaoka M (1994) *Tetrahedron Lett* **35**: 2183
- [33] Palazoin JM, Martin VS (1995) *Tetrahedron Lett* **36**: 3549
- [34] Paquette LA, Sweeney TJ (1990) *J Org Chem* **55**: 1703
- [35] Nicolaou KC, McGarry DG, Somers PK, Kim BH, Ogilvie WW, Yiannikouros G, Prasad CVC, Veale CA, Hark RR (1990) *J Am Chem Soc* **112**: 6263
- [36] Carling RW, Clark JS, Holmes AB (1992) *J Chem Soc Perkin Trans* **1**: 83
- [37] Carling RW, Clark JS, Holmes AB, Sartor D (1992) *J Chem Soc Perkin Trans* **1**: 95
- [38] Fuhry MA, Holmes AB, Marshall DR (1993) *J Chem Soc Perkin Trans* **1**: 2743
- [39] Alvarez E, Diaz MT, Pérez R, Ravelo JL, Requeiro A, Vera JA, Zurita D, Martin JD (1994) *J Org Chem* **59**: 2848
- [40] Bugarcic Z, Konstantinovic S, Mojsilovic B (1999) *Ind J Chem* **38B**: 728
- [41] Petrovic Z, Mojsilovic B, Bugarcic Z (2001) *J Mol Cat A: Chem* **170**: 267
- [42] Mojsilovic B, Bugarcic Z (2001) *Heteroatom Chem* **12**: 475