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An Improved Procedure for Phenylselenoetherification of Some Δ^5 -Alkenols Using Pyridine, Ag_2O , and Some Lewis Acids as Catalysts

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ABSTRACT: An improved procedure for intramolecular cyclization of some Δ^5 -alkenols, using PhSeX ($X = \text{Cl}, \text{Br}$) has been developed. We found that cyclization can be facilitated in the presence of pyridine, Ag_2O , and some Lewis acids as catalysts. Thus catalytic amount of additives (pyridine and Ag_2O) influences higher yields but equimolar amount achieves almost quantitative yield under extremely mild experimental conditions. In the presence of Lewis acids (ZnCl_2 and FeCl_3) high yields of cyclic ether products are obtained with catalytic amounts. © 2004 Wiley Periodicals, Inc. *Heteroatom Chem* 15:146–149, 2004; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10227

INTRODUCTION

During the last years, cyclic ether units are important synthetic targets in organic and medicinal chemistry due to their widespread occurrence in many complex natural compounds exhibiting important biological activity [1]. These units can be found isolated

in monocyclic or polycyclic compounds, fused with other cyclic ethers or forming spiro systems [2]. The presence in nature of molecules with oxygenated heterocycles is receiving considerable attention considering their capacity of modification of the transport of the metal cations Na^+ , K^+ , and Ca^{2+} through the lipid membranes [3–6], this activity being 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], etc.

A number of synthetic 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 cyclic precursor [35–41].

EXPERIMENTAL

All reactions were carried out on a 1 mmol scale. To a magnetically stirred solution of alkenol (1 mmol) and catalyst (0.1 mmol or 1 mmol) in dry dichloromethane (5 cm^3), solid PhSeCl (0.212 g, 1.1 mmol) or PhSeBr (0.260 g, 1.1 mmol) was added at room temperature. The reaction went to completion in a few minutes. The pale yellow solution was washed (in the case of pyridine as a catalyst) with 1 M HCl aqueous solution (5 cm^3), saturated NaHCO_3 , and then brine or with saturated NaHCO_3 and water (in the case of Ag_2O , ZnCl_2 , and FeCl_3). The organic

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layer was dried over Na_2SO_4 , concentrated and chromatographed. The product was obtained after the eluation of the traces of diphenyl diselenide from a silica gel-dichloromethane column. All the products were characterized and identified on the basis of their spectral data. The cyclic ether products were known compounds, and their spectral data had been given previously [29].

RESULTS AND DISCUSSION

In recent years, we have studied intramolecular cyclization of some Δ^4 - and Δ^5 -alkenols by means of phenylselenenyl halides [30–41], PhSeX ($\text{X} = \text{Cl}, \text{Br}$). 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 with PhSeCl . Although the additional 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, we presented an approach to cyclic ethers from tertiary alkenols using PhSeX ($\text{X} = \text{Cl}, \text{Br}$) in the presence of pyridine [42]. Procedure works smoothly resulting in quantitative formation of the cyclic ethers. Prompted by this finding we considered it synthetically interesting and profitable for our purposes to extend this method to other representative alkenols in order to describe a general procedure for a rapid and efficient cyclization reaction of alkenols with phenylselenenyl halides. In this paper, we wish to present the extension of the method to primary and secondary Δ^5 -alkenols and with Ag_2O , ZnCl_2 , and FeCl_3 as catalysts. These alkenols afforded tetrahydropyran derivatives, which are commonly encountered substructures in many natural products showing interesting biological properties, the most prominent of these being polyether antibiotics (such as monensin, narasin, and tetrinomycin), marine toxins, and pheromones [3]. Hence, of particular importance is the discovery of the appropriate experimental conditions under which phenylselenocyclization of Δ^5 -alkenols would readily be accomplished in synthetically useful manner, regardless of the reagent used. The results of our investigation are shown in Table 1 and in Scheme 1.

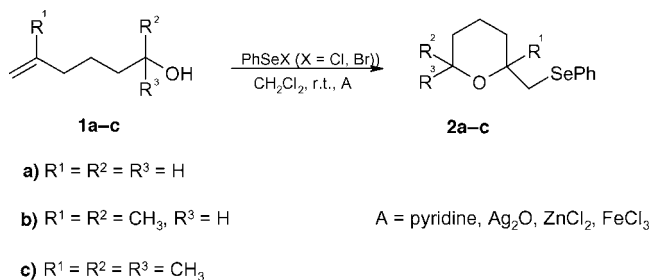
All reactions proceeded to form oxygen heterocycles bearing the phenylseleno moiety. Cyclization is facilitating by the presence of pyridine, Ag_2O , and some Lewis acids (ZnCl_2 and FeCl_3). It became clear that phenylselenenyl halides in combination with these catalysts usually gave rise to cleaner reactions

TABLE 1 Yields (%) of Cyclic Ethers **2a–c** from the Phenylselenoetherification of Some Δ^5 -Alkenols in the Presence of a Catalytic and Equimolar Amount of Pyridine and Ag_2O , and a Catalytic Amount of ZnCl_2 and FeCl_3

	2a	2b	2c
PhSeCl	81	80	31
PhSeCl , pyridine cat.	90	86	54
PhSeCl , pyridine equ.	100	100	100
PhSeCl , Ag_2O cat.	98	90	69
PhSeCl , Ag_2O equ.	100	100	96
PhSeCl , ZnCl_2 cat.	100	94	89
PhSeCl , FeCl_3 cat.	100	92	86
PhSeBr	75	26	0
PhSeBr , pyridine cat.	79	63	36
PhSeBr , pyridine equ.	100	100	100
PhSeBr , Ag_2O cat.	86	78	55
PhSeBr , Ag_2O equ.	98	97	87
PhSeBr , ZnCl_2 cat.	100	81	78
PhSeBr , FeCl_3 cat.	100	91	87

and improved yields compared with phenylselenenyl halides alone.

Also, the additives increased the reaction rate dramatically; all reactions were completed a few minutes (without additives reaction time is half an hour to several hours). Although the reactions in the presence of pyridine and Ag_2O can be performed in a catalytic manner, we found that almost quantitative yields were obtained when 1 equivalent amount of additive was used (Table 1). As we can see from the results, pyridine shows the best results in the case of equimolar amount, while Ag_2O is a better catalyst for this type of cyclization. In the case of the tertiary alkenol with more substituents (**1c**) the product yield decreases because of the effects of steric hindrance. Depending on the mechanism, this can indeed be expected. It appears that the presence of pyridine is beneficial to the cyclization process and more likely due to its basic properties. Subsequently, we evaluated the effect of some Lewis acids on the cyclization process. The results obtained indicate that the presence of ZnCl_2 and FeCl_3 plays a crucial role in the cyclization process (Table 1). Yields



SCHEME 1

of the cyclic ether products in the presence of catalytic amount of ZnCl_2 and FeCl_3 are even better than those obtained with pyridine and Ag_2O . Even though PhSeCl in combination with equimolar amount of ZnCl_2 is known as a strong chlorophenylselenylating agent for olefins [43], in phenylselenocyclization reaction of our alkenols presence of equimolar amount of ZnCl_2 and FeCl_3 influenced moderate yields (41–99%).

We also evaluated the effect of AgOAc on the cyclization process. The results obtained indicate that in the presence of AgOAc (in catalytic and equimolar amount) the cyclization process is slower and yields of the phenylseleno ethers are lower (27–86% in catalytic amount and 42–89% in equimolar amount).

These results are clear evidence that the presence of pyridine, Ag_2O , ZnCl_2 , and FeCl_3 increase the yield of the cyclic ether products.

A speculative rationale explaining the increased yields of cyclic ether products in the additive-catalyzed process performed under our conditions could be the following. All used additives can bound counter ion from reagent (X^- from PhSeX), increase electrophilicity of PhSe group, and eliminate X^- as a concurrent of hydroxyl group in cyclization step. All additives could enhance the nucleophilicity of the hydroxyl group of the alkenol and also mediate the stabilization of the oxonium ion intermediates.

In conclusion, it appears that the above described conditions for cyclization of Δ^5 -alkenols to THP-ethers are more advantageous in terms of time and yield than those previously reported for the same reagents [44]. In addition, other conditions will be tested to increase the yields for the less effective alkenols.

This improved procedure for phenylselenoetherification should often prove the simplest and superior to those currently available. As for the yields of cyclic ethers, the procedure described in this article 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. Moreover, we are confident that this procedure will be of general use for a facile synthesis of various heterocycles.

We believe that this point and the possible mechanistic implications are worthy of further studies.

REFERENCES

- [1] Yasumoto, T.; Murata, M. *Chem Rev* 1993, 93, 1897.
- [2] Faulkner, D. *J Nat Prod Rep* 1997, 14, 259.
- [3] Wesley, J. W. *Polyether Antibiotics Naturally Occurring Acid Ionophores*; Marcel Dekker: New York, 1982; Vols. I and II.
- [4] Painter, G. R.; Presman, B. C. *Top Curr Chem* 1982, 101, 83.
- [5] Still, W. C.; Hauck, P.; Kempf, D. *Tetrahedron Lett* 1987, 28, 2817.
- [6] Smith, P. W.; Still, W. C. *J Am Chem Soc* 1988, 110, 7917.
- [7] Shimizu, Y. *Marine Natural Products*; Academic Press: New York, 1978; Vol. I, p. 1.
- [8] Ellis, S. *Toxicon* 1985, 23, 469.
- [9] Sakemi, S.; Higa, T.; Jefford, C. W.; Bernardinelli, G. *Tetrahedron Lett* 1986, 27, 4287.
- [10] Suzuki, T.; Suzuki, A.; Furusaki, T.; Matsumoto, A.; Kato, A.; Imanaka, Y.; Kurosawa, E. *Tetrahedron Lett* 1985, 26, 1329.
- [11] Corley, D. G.; Herb, R.; Moore, E.; Scheuer, P. J.; Paul, V. J. *J Org Chem* 1988, 53, 3644.
- [12] Cohran, V. M. *Physiology of Fungi*; Wiley: New York, 1958.
- [13] Schreiber, S. L.; Kelly, S. E.; Porco, J. A.; Sanmakia, T.; Suh, E. M. *J Am Chem Soc* 1988, 110, 6210.
- [14] González, A. G.; Martin, J. D.; Martin, V. S.; Norte, M.; Pérez, R.; Ruano, J. Z.; Drexler, S. A.; Clardy, J. *Tetrahedron* 1982, 38, 1009.
- [15] Ravelo, J. L.; Regueiro, A.; Martin, J. D. *Tetrahedron Lett* 1992, 33, 3389.
- [16] Hoffmann, R. W.; Münster, I. *Tetrahedron Lett* 1995, 36, 1431.
- [17] Alvarez, E.; Diaz, M. T.; Hanxing, L.; Martin, J. D. *J Am Chem Soc* 1995, 117, 1437.
- [18] Clark, J. S.; Kettle, J. G. *Tetrahedron Lett* 1997, 38, 127.
- [19] Inoue, M.; Sasaki, M.; Tachibana, K. *Tetrahedron Lett* 1997, 38, 1611.
- [20] Berger, D.; Overman, L. E.; Renhowe, P. A. *J Am Chem Soc* 1997, 119, 2446.
- [21] Crimmins, M. T.; Choy, A. L. *J Org Chem* 1997, 62, 7548.
- [22] Nicolaou, K. C.; Prasad, C. V. C.; Hwang, C. K.; Duggan, M. E.; Veale, C. A. *J Am Chem Soc* 1989, 111, 5321.
- [23] Nicolaou, K. C.; Prasad, C. V. C.; Somers, P. K.; Hwang, C. K. *J Am Chem Soc* 1989, 111, 5330.
- [24] Nicolaou, K. C.; Prasad, C. V. C.; Somers, P. K.; Hwang, C. K. *J Am Chem Soc* 1989, 111, 5335.
- [25] Cooper, A. J.; Salomon, R. G. *Tetrahedron Lett* 1990, 31, 3813.
- [26] Suzuki, T.; Sato, O.; Hirama, M. *Tetrahedron Lett* 1990, 31, 4747.
- [27] Aicher, T. D.; Buszek, K. R.; Fang, F. K.; Forsyth, C. J.; Jung, S. H.; Kishi, Y.; Scola, P. M. *Tetrahedron Lett* 1992, 33, 1549.
- [28] Martin, V. S.; Polazón, J. M. *Tetrahedron Lett* 1992, 33, 2399.
- [29] Konstantinovic, S.; Bugarčić, Z.; Milosavljevic, S.; Schroth, G.; Mihailovic, M. Lj. *Liebigs Ann Chem* 1992, 261.
- [30] Gung, B. W.; Francis, M. B. *J Org Chem* 1993, 58, 6177.
- [31] Mukai, C.; Ikeda, Y.; Sugimoto, Y.; Hanaoka, M. *Tetrahedron Lett* 1994, 35, 2179.
- [32] Mukai, C.; Sugimoto, Y.; Ikeda, Y.; Hanaoka, M. *Tetrahedron Lett* 1994, 35, 2183.

- [33] Palazoin, J. M.; Martin, V. S. *Tetrahedron Lett* 1995, 36, 3549.
- [34] Paquette, L. A.; Sweeney T. J. *J Org Chem* 1990, 55, 1703.
- [35] Nicolaou, K. C.; McGarry, D. G.; Somers, P. K.; Kim, B. H.; Ogilvie, W. W.; Yiannikouros, G.; Prasad, C. V. C.; Veale, C. A.; Hark, R. R. *J Am Chem Soc* 1990, 112, 6263.
- [36] Carling, R. W.; Clark, J. S.; Holmes, A. B. *J Chem Soc, Perkin Trans 1* 1992, 83.
- [37] Carling, R. W.; Clark, J. S.; Holmes, A. B.; Sartor, D. J. *J Chem Soc, Perkin Trans 1* 1992, 95.
- [38] Fuhry, M. A.; Holmes, A. B.; Marshall, D. R. *J Chem Soc, Perkin Trans 1* 1993, 2743.
- [39] Alvarez, E.; Diaz, M. T.; Pérez, R.; Ravelo, J. L.; Requeiro, A.; Vera, J. A.; Zurita, D.; Martin, J. D. *J Org Chem* 1994, 59, 2848.
- [40] Bugarcic, Z.; Konstantinovic, S.; Mojsilovic, B. *Indian J Chem* 1999, 38B, 728.
- [41] Petrovic, Z.; Mojsilovic, B.; Bugarcic, Z. *J Mol Cat A: Chem* 1999, 142, 393.
- [42] Mojsilovic, B.; Bugarcic, Z. *Heteroat Chem* 2001, 12, 475.
- [43] D'Onofrio, F.; Parlanti, L.; Piancatelli, G. *Tetrahedron Lett* 1995, 36, 1929.
- [44] Tiecco, M. *Electrophilic Selenium, Selenocyclizations, Topics in Current Chemistry*; Springer-Verlag: Wien, 2000; Vol. *Organoselenium Chemistry: Modern developments in Organic Synthesis*, pp. 7–54.