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Benzeneseleninic acid in the photo-catalyzed hydroxy-selenylation of styrenes

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Abstract: We established a new visible-light-mediated protocol for the regioselective β-hydroxyselenilation of olefins, employing benzeneseleninic acid as substrate. Regarding a novel approach, the bezeneseleninic acid emerges as an efficient and affordable reagent to be used as electrophilic selenium source, besides to be easily converted to selenium-based radical species under visible-light conditions. In this sense, the photocatalytically formed PhSe• radical can react directly with unsaturated substrates, including alkenes, to access a new C-Se bond and a carbon-centered radical intermediate, which finally is trapped by a hydroxyl radical specie, delivering the β-hydroxyselanyl compounds. Thus, despite the versatile utilities in organic synthesis as building blocks, the β-hydroxyselanyl have demonstrated important biological activities. Based on that, we concentrated our efforts to develop a robust, effective, and environmentally benign methodology for their preparation. The optimal condition involves the reaction between styrene and 1.0 equivalent of phenylseleninic acid, in the presence of 5.0 mol% of eosin Y, as a cheap and easily available photocatalyst, with DMSO promoting the reaction medium. Satisfactorily, the system was irradiated with blue LED light for 2 hours, to deliver the desired products in good yields.

Keywords: visible-light; photocatalysis; benzeneseleninic acid; β-hydroxyselanyl

1. Introduction

β-hydroxyselanyl derivatives have valuable structural functions, appearing in a variety of drug candidates, biologically active compounds and advanced organic synthetic materials [1,2]. They also act as an important synthetic intermediate for the construction of natural products, such as pancratistatin [3], sphingosine [4], and schweinfurthin B [5]. Additionally, β-hydroxy selenides have been employed smoothly as substrate to access allylic alcohols [6], olefins [7], bromohydrins [8], and oxygen-containing heterocycles [9].

There are, on the literature, several methods to prepare these compounds. The most conventional involves the ring-opening reactions of epoxides with the selenolate anions (RSe^-), which can be generated *in situ* from diselenides [10] or from elemental selenium [12]. However, long reaction times, limited substrate scope and poor regioselectivity are among the common drawbacks found in these protocols. Thus, recently several alternative protocols for synthesis of β-hydroxy selenides have been emerging. Among them, the regioselective direct hydroxyselenation of active olefins, with diselenides [13-15], has proven to be a highly effective and robust strategy to prepare β-hydroxy selenides. However, the use of benzeneseleninc acids, as a bench-stable electrophilic Se-based source, is still scarce [16].

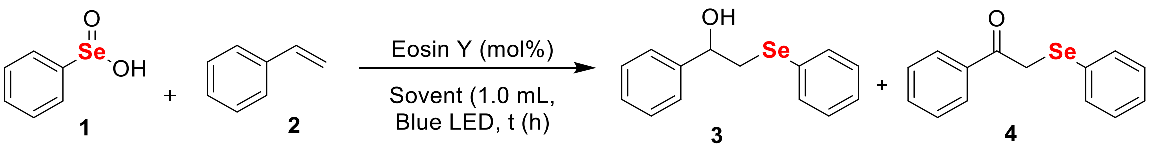
On the other hand, the use of alternative energy sources has become a remarkable factor in organic synthesis, in order to circumvent the use of oil-based energies. In this context, several methods involving the hydroxyselenation of olefins have been using alternative energy sources, including microwave irradiation [17], ultrasonic irradiation [18], and electricity [19].

Based on that, herein describe a robust, effective, and environmentally benign methodology for preparation β-hydroxyselenenylation of olefins, employing benzeneseleninic acids as bench-stable Se-based electrophile, under a photocatalytic system.

2. Results and Discussion

Firstly, in a reaction flask were added benzeneseleninic acid **(1)** (0.3 mmol), styrene **(2)** (1.0 equiv.), the organic photocatalyst eosin Y (5 mol%) and dimethylsulfoxide (DMSO, 1.0 mL). The resulting mixture was stirred for 1 hour, at room temperature, under blue LED irradiation. At the end, the desired product **3** was obtained in 65% yield (Table 1, entry 1). Parallelly, a trace amount of the *β*-selenoketone **4**, was obtained as byproduct. Then, in order to drive the reaction toward the product **3**, longer reaction times were evaluated (Table, entries 2-4). In 2 hours, the product 3 was obtained in 73%, with an overall yield of 84%. However, a slight decrease in the reaction selectivity was observed when the mixture was irradiated for 4 hours, affording an overall yield of 81% with 65% of the product **3**. Thus, based on these observations, 2 hours was elected as the best reaction time to obtain compound **3** efficiently. Thus, a range of different organic solvents were employed to promote the reaction medium, however none of them delivered better results (Table 1, entries 5-10).

Table 1. Optimization of Reaction Conditions.[a]



Entry	Solvent	Time (h)	Yield 3 (%)[b]	Yield 4 (%)[b]
1	DMSO	1	65	Trace
2	DMSO	2	73	11
3	DMSO	4	65	16
4	DMSO	24	56	21
5	DCM	2	-	18
6	MeCN	2	14	21
7	THF	2	15	4
8	PEG 400	2	7	Trace
9	DMF	2	25	4
10	Ethyl Acetate	2	9	-
11[c]	DMSO	2	13	Trace
12[d]	DMSO	2	44	5
13[e]	DMSO	2	-	-

Reaction conditions a): In a specific reaction tube were added 0.3 mmol of Benzeneseleninic acid **(1)**, 0.3 mmol of styrene **(2)**, 5 mol% of Eosin Y, as a photocatalyst, and solvent (1.5 mL). The mixture reaction was stirring at the room temperature under blue LED light irradiation (50 W). The reactions time ware monitored by TLC. b) Isolated yields obtained by chromatographic column. c) Reaction performed with 3 mol% of Eosin Y. d) Reaction performed with 10 mol% of Eosin Y. e) Reaction performed without Eosin Y.

Thus, eosin Y was employed in 3 and 10 mol%, however the access to the product **3** has been negatively affected (Table 1, entries 11-12). Finally, in order to prove that the use of eosin Y is mandatory for the reaction success, an experiment was carried out in the absence of catalyst, in which almost all substrates were recovered at end (Table 1, entry 13). In addition, was possible to observe the formation of a small amount of diphenyl diselenide, resulting from benzeneseleninic acid oxidation. Based on that, until the moment the best reaction condition was defined by reacting the substrates **1** and **2** for 2 hours, in the presence of DMSO and under blue LED light irradiation at room temperature, affording the desired *β*-hydroxy selenide **3** in 73% yield (Table 1, entry 3).

3. Conclusion

In conclusion, we have developed a simple and efficient approach for the β-hydoxyselenylation of styrenes, employing benzeneseleninic acids, as an efficient Se-based source, presenting a good regioselectivity toward the *β*-hydroxy selenide **3**. It is worth to mention that some studies are still occurring on our laboratory, including the influence other wavelength sources and the reaction substrate scope, as well as the search for evidences to clarify each step of the reaction mechanism.

4. General Information

The reactions were irradiated by blue LED ligth (50 W) and monitored by TLC carried out on pre-coated TLC sheets ALUGRAM® Xtra SIL G/UV254 by using UV light as visualization agent and the mixture of 5% vanillin in 10% H_2SO_4 under heating conditions as developing agent. The purification was performed by flash chroma-tography employing Merck silica gel (particle size 63–200 μm), as a stationary phase. Hydrogen nuclear magnetic resonance spectra (^{1}H NMR) were obtained at 400 MHz on Bruker Ascend 400 spectrometer. The spectra were recorded in $CDCl_3$ solutions. The chemical shifts are reported in ppm, referenced to tetramethysilane (TMS) as the external reference. Hydrogen coupling patterns are described as singlet (s), doublet (d), triplet (t), doublet of doublets (dd), and multiplet (m). Coupling constants (*J*) are reported in Hertz. Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained at 100 MHz on Bruker Nuclear Ascend 400 spectrometer. The chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$

General procedure for synthesis of β-hydroxyselanyl compound 3a: In a specific reaction tube was added 0.3 mmol of benzeneseleninic acid (**1**), 0.3 mmol of styrene (**2**), 5 mol% of photocatalyst Eosin Y and 1.0 mL of DMSO. The reaction was stirred for 2 hours at room temperature under blue LED visible light. After the reaction time, the solvent was completely removed under vacuum to give the crude. The product was purified by column chromatographic using silica gel as stationary phase and a mixture of ethyl acetate and hexane (20:80) as mobile phase. The desired compound **3** and the by-product **4** was characterized by NMR analysis.

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References

[1] Tanini, D.; Capperucci, A.; Degl'Innocenti, A. Bis(trimethylsilyl)selenide in the Selective Synthesis of β-Hydroxy, β-Mercapto, and β-Amino Diorganyl Diselenides and Selenides Through Ring Opening of Strained Heterocycles. *Eur. J. Org. Chem*. **2015**, 357–369.

[2] Back, T. G.; Moussa, Z. Diselenides and Allyl Selenides as Glutathione Peroxidase Mimetics. Remarkable Activity of Cyclic Seleninates Produced in Situ by the Oxidation of Allyl ω-Hydroxyalkyl Selenides. *J. Am. Chem. Soc*. **2003**, *125*, 13455–13460.

[3] Rigby, J, H.; Maharoof, U. S. M.; Mateo, M. E. Studies on the Narciclasine Alkaloids: Total Synthesis of (+)-Narciclasine and (+)-Pancratistatin *J. Am.Chem. Soc*. **2000**. *122*, 6624–6628.

[4] Azuma, H.; Tamagaki, S.; Ogino, K. Stereospecific Total Syntheses of Sphingosine and Its Analogues from l-*Serine J. Org. Chem*. **2000**, *65*, 3538–3541.

[5] Treadwell, E. M.; Neighbors, J. D.; Wiemer, D. F. A Cascade Cyclization Approach to Schweinfurthin B. *Org. Lett*. **2002,** *4*, 3639–3642.

[6] Sharpless, K. B.; Lauer, R. F. Mild Procedure for the Conversion of Epoxides to Allylic Alcohols. First organoselenium reagent. *J. Am. Chem. Soc*. **1973**, *95*, 2697–2699.

[7] Remion, j.; Dumont, W.; Krief, A. New Regiospecific Routes to Olefins from β-hydroxy selenides. *Tetrahedron Lett*. **1976**, *17*, 1385–1388.

[8] Sevring, M.; W. Dumont, W.; Hevesi, L.; Krief, A. Transformation of Selenides to Alkylhalides. New routes for Homologization of Primary Alkylhalides. *Tetrahedron Lett*. **1976**, *17*, 2647.

[9] M. Gruttadauri, R. Noto, Kinetic and Thermodynamic Control in the Intramolecular Hydroxyl Capture of Seleniranium ions. *Tetrahedron Lett*. **1999**, *40*, 8477–8481.

[10] Yang, M.; Zhu, C.; Yuan, F.; Huang, Y.; Pan, Y. Enantioselective Ring-Opening Reaction of meso-Epoxides with ArSeH Catalyzed by Heterometallic Ti−Ga−Salen System. *Org. Lett*. **2005**, *7*, 1927–1930.

[11] V. Ganesh, V.; Chandrasekaran, S. One-Pot Synthesis of β-Amino/β-Hydroxy Selenides and Sulfides from Aziridines and Epoxides. *Synthesis.* **2009**, *19*, 3267–3278

[12] Leng, T.; Wu, G.; Zhou, Y-B.; Gao, W.; Ding, J.; Huang, X.; Liu, Mi.; Wua, H. Silver-Catalyzed One-Pot Three-Component Selective Synthesis of β-Hydroxy Selenides. *Adv. Synth. Catal.* **2018**, *360*, 4336–4340.

[13] Perin, G.; Santoni, P.; Barcellos, A. M.; Nobre, P. C.; Raquel G. Jacob, R. G.; Lenardão, E. J.; Santi, C. Selenomethoxylation of Alkenes Promoted by Oxone®. *Eur. J. Org. Chem.*, **2018**, *10*, 1224–1229.

[14] Zhang, Y.; Wu, S.; Yan, J. New Catalytic Method for the Synthesis of β-Hydroxy Selenides. *Helv. Chim. Acta*. **2016**, *99*, 654–658

[15] Wang, X-L.; Li, H-J.; Yan, J. Iodine-mediated Regioselective Hydroxyselenenylation of Alkenes: Facile Access to β-hydroxy selenides. *Chinese Chem. Lett.* **2018**, *29*, 479–481.

[16] Hori, T.; K. Sharpless, B. Synthetic Applications of Arylselenenic and Arylseleninic Acids. Conversion of Olefins to Allylic Alcohols and Epoxides. *J. Org. Chem*. **1978**, *43*, 1689–1697.

[17] Chenga, T.; Zheng, X.; Ke, Q. Ultrasound Assisted Ring-opening Reaction of Epoxides with 1,2-diphenyldiselenide. J. *Chem. Res.* **2011**, *29*, 522–524.

[18] Vieira, A. A.; Azeredo, J. B.; Godoi, M.; Santi C.; Silva Júnior, E. N. da.; Braga, A. L. Catalytic Chalcogenylation under Greener Conditions: A Solvent-Free Sulfur- and Seleno-functionalization of Olefins via I_2/DMSO Oxidant System. *J. Org. Chem.* **2015**, *80*, 2120–2127

[19] Sun, L.; Yuan, Y.; Yao, M.; Wang, H.; Wang, D.; Gao, M.; Yi-Hung Chen, Y-H.; Lei, A. Electrochemical Aminoselenation and Oxyselenation of Styrenes with Hydrogen Evolution *Org. Lett.* **2019**, 21,1297–1300.