Hindawi Publishing Corporation
Journal of Chemistry
Volume 2016, Article ID 2849140, 8 pages
http://dx.doi.org/10.1155/2016/2849140

Research Article

Reaction of Acyl Chlorides with *In Situ* Formed Zinc Selenolates: Synthesis of Selenoesters *versus* Ring-Opening Reaction of Tetrahydrofuran

Gemma Bellino,[1] Marialaura Scisciani,[1] Jaqueline Pinto Vargas,[2] Luca Sancineto,[1] Luana Bagnoli,[1] Francesca Marini,[1] Diogo Seibert Lüdtke,[2] Eder Joao Lenardao,[3] and Claudio Santi[1]

[1]*Group of Catalysis and Organic Green Chemistry, Department of Pharmaceutical Sciences, University of Perugia, Via del Liceo 1, 06100 Perugia, Italy*
[2]*Instituto de Química, Universidade Federal do Rio Grande do Sul (UFRGS), Avenida Bento Gonçalves 9500, 91501-970 Porto Alegre, RS, Brazil*
[3]*Laboratório de Síntese Orgânica Limpa (LASOL), Centro de Ciências Químicas, Farmacêuticas e de Alimentos (CCQFA), Universidade Federal de Pelotas (UFPel), P.O. Box 354, 96010-900 Pelotas, RS, Brazil*

Correspondence should be addressed to Claudio Santi; claudio.santi@unipg.it

Received 2 March 2016; Accepted 24 May 2016

Academic Editor: Matthias D'hooghe

Attempting to apply the *in situ* production of PhSeZnSePh to the synthesis of selenoesters, an unexpected reaction involving the solvent (tetrahydrofuran) was observed and studied. We reported here some evidences about the mechanism and the possibility to control the chemoselectivity of this new reaction that afforded the formation of interesting selenoderivatives in which the selenium moiety and the carboxylic one are spaced by four carbon units.

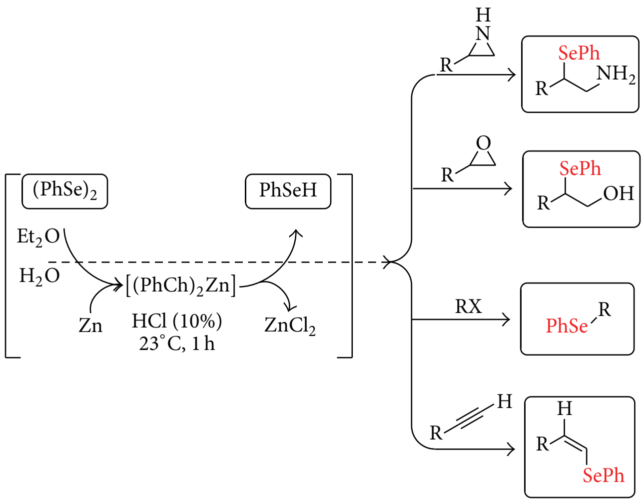
1. Introduction

Given the continuous interest around the synthesis, the reactivity, and the biological properties of organochalcogen compounds and continuing our ongoing studies on the development of new ecofriendly protocols for the selenenylation of organic substrates, we investigated a new strategy for the preparation of selenoesters [1–4].

The incorporation of selenium into organic compounds can be conveniently achieved using nucleophilic reagents such as selenols or selenolates, which can be generated *in situ* via a reductive cleavage of the Se-Se bond starting from a diselenide. Commonly used protocols for generating selenolates involve the use of several reducing agents, such as $NaBH_4$, $LiAlH_4$, and other expensive and often not easily handled metal sources [5–8].

We recently demonstrated that elemental zinc reduces diselenides in acidic biphasic system (aq. 10% HCl/Et_2O) affording *in situ* a seleno-zinc complex (in equilibrium with the corresponding selenol) that can be conveniently used to effect ring-opening reactions of aziridines [9] and epoxides, as well as nucleophilic substitution [10] and hydroselenylation of alkynes [11] (Scheme 1). The novelty of this protocol is mainly related to the simplicity of the procedure that prevents the typical drawback of using volatile selenols, which has a persistent smell. In this case, the selenol is formed in a closed vial and immediately used for the reaction with the electrophile. We also demonstrated that, in some cases, the water and the organic phase can be recovered after the first reaction and directly reused as medium for further reactions, maintaining good yields for 5–10 cycles. This aspect positively impacts the overall sustainability of the reaction [12].

Starting from diphenyl diselenide, the discoloration of the organic phase is an unequivocal indication of the complete reduction of the Se-Se bond and the formation of the zinc complex that, due to the presence of the hydrochloric acid,



Scheme 1

is most reasonably in equilibrium with the corresponding benzeneselenol.

During the attempts to apply this methodology to the synthesis of selenol esters, starting from the corresponding acyl chlorides, in order to avoid the presence of strong hydrolytic conditions, we tested tetrahydrofuran (THF) as solvent and triflic acid as anhydrous acidic catalyst for the reduction. Serendipitously, we discovered that in these conditions the ring-opening reaction of THF was favored. Ring-opening reaction of cyclic tetrahydrofuran is an important synthetic transformation because it affords a functionalized 4-carbon building block that can be used in many synthetic applications including polymer chemistry. In addition, a reaction able to break a carbon-oxygen bond of an ether presents potentially useful applications in the decomposition of polyether based polymers and, consequently, in the treatment of the wastes for the production of new functionalized chemicals [12–15].

2. Materials and Methods

Reactions were conducted in round bottom flasks and were stirred with Teflon-coated magnetic stirring bars. Solvents and reagents were used as received unless otherwise noted. Acyl chlorides **1a**, **1d**, and **1g** were commercially available; acyl chlorides **1b**, **1c**, **1e**, and **1f** were synthesized according to the literature [16]. Analytical thin-layer chromatography (TLC) was performed on silica gel 60 F254 precoated aluminum foil sheets and visualized by UV irradiation or by iodine staining. Silica gel Kieselgel 60 (70–230 mesh) was used for column chromatography. NMR experiments were conducted at 25°C with a Bruker DPX 200 spectrometer operating at 200 MHz for ^{1}H and 50.31 MHz for ^{13}C, or with a Bruker DRX spectrometer operating at 400 MHz for ^{1}H and 100.62 MHz for ^{13}C experiments.

^{1}H and ^{13}C chemical shifts (δ) are reported in parts per million (ppm), relative to TMS ($\delta = 0.0$ ppm) and the residual solvent peak of $CDCl_3$ ($\delta = 7.26$ and 77.00 ppm in ^{1}H and ^{13}C NMR, resp.). Data are reported as chemical shift (multiplicity, coupling constants where applicable, number of hydrogen atoms, and assignment where possible). Abbreviations are s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), sex (sextet), dd (doublet of doublet), dt (doublet of triplet), ddt (doublet of doublet of triplet), m (multiplet), and br. s (broad signal). Coupling constant (J) is quoted in hertz (Hz) to the nearest 0.1 Hz. GC-MS analyses were carried out with a HP-6890 gas chromatograph (dimethyl silicone column, 12.5 m) equipped with an HP-5973 mass-selective detector.

2.1. General Procedures for the Synthesis of Selenoester in Biphasic Conditions. Diphenyl diselenide (0.637 mmol) was poured into a biphasic system composed of Et_2O (2 mL) and HCl (aq. 10%, 2 mL) and zinc pellets (20 eq.) were added. The mixture was vigorously stirred (800 rpm) in a closed vial until discoloration of the organic layer (around 15 min).

Acyl chlorides **1a**–**g** (1.274 mmol) were added and the mixture was stirred at room temperature for 4 h. The organic phase was diluted with EtOAc (2 mL), separated, dried with Na_2SO_4, and filtered and the solvent was removed under vacuum. The products reported in Table 1 were purified by flash chromatography on silica gel (PE/EtOAc: 96/4) and characterized on the basis of ^{1}H-NMR, ^{13}C-NMR, and GC-MS spectral analysis.

2.2. General Procedure for the Synthesis of Selenoester in THF. In a round bottom flask, containing diphenyl diselenide (0.25 mmol) and zinc powder (0.458 mmol) in dry THF (3 mL) under argon atmosphere, trifluoromethanesulfonic acid (30 mol%) was added as the catalyst. The resulting mixture was refluxed for 1 h, observing the formation of a white suspension. After cooling to room temperature, the acyl chloride (**1a**–**g**, 0.5 mmol) was added, and the mixture was stirred for an additional 1.5 h at refluxing temperature. The crude was then extracted with ethyl acetate (3x 10 mL) and the organic layers were washed with brine (10 mL) and dried over Na_2SO_4. After filtration, the organic solvent was removed under reduce pressure. Products **3**, **6,** and **7** were purified by flash chromatography on silica gel (PE/EtOAc: 96/4) and characterized by ^{1}H-NMR and ^{13}C-NMR spectra.

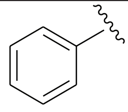
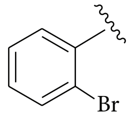
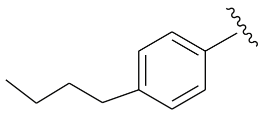
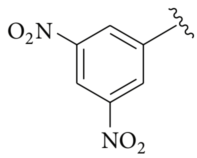
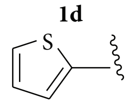
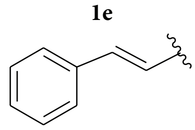
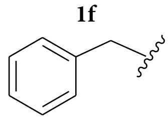
Physical and spectroscopic data of selected compounds are reported below.

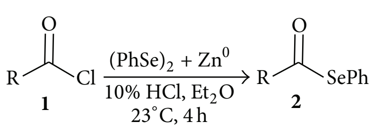
*Se-phenyl benzoselenoate (**2a**): ^{1}H-NMR* ($CDCl_3$, 200 MHz): δ = 7.96–7.92 (m, 2H, H-Ar), 7.63–7.42 (m, 8H, H-Ar) ppm. *^{13}C-NMR* ($CDCl_3$, 50 MHz): δ = 193.5, 138.5, 136.4, 133.9, 129.4, 129.1, 128.9, 127.4, 125.8 ppm. *GC-MS*: *m/z* (%) = 262 (1) [M$^+$], 157 (5), 105 (100), 77 (50), 51 (14).

*Se-phenyl 2-bromobenzoselenoate (**2b**): ^{1}H-NMR* ($CDCl_3$, 200 MHz): δ = 7.72–7.6 (m, 4H, H-Ar), 7.45–7.34 (m, 5H, H-Ar) ppm. *^{13}C-NMR* ($CDCl_3$, 50 MHz): δ = 194.4, 140.6, 135.8, 134.3, 132.6, 129.5, 129.2, 128.8, 127.3, 126.6, 118.0 ppm. *GC-MS*: *m/z* (%) = 340 (1) [M$^+$], 232 (3), 183 (100), 157 (54), 76 (16), 50 (9).

*Se-phenyl 4-butylbenzoselenoate (**2c**): ^{1}H-NMR* ($CDCl_3$, 200 MHz): δ = 7.85 (d, J = 8.1 Hz, 2H, H-Ar), 7.61–7.57 (m, 2H, H-Ar), 7.44–7.41 (m, 3H, H-Ar), 7.31–7.26 (m, 2H, H-Ar), 2.67 (t, J = 7.8 Hz, 2H, CH_2), 1.61 (quin, J = 8.15 Hz, 2H, CH_2), 1.36 (sex, J = 7.6 Hz, 2H, CH_2), 0.95 (t, J = 7.2 Hz, 3H, CH_3) ppm. *^{13}C-NMR* ($CDCl_3$, 100 MHz): δ = 192.7, 149.8, 136.4, 136.2,

Table 1: Scope of the reaction (see Scheme 2).

Entry	R	Yield% of **2**
1	 **1a**	37
2	 **1b**	52
3	 **1c**	84
4	 **1d**	Mixture of unidentified compounds
5	 **1e**	23
6	 **1f**	0
7	 **1g**	0



Scheme 2

129.3, 129.0, 127.5, 126.0, 35.8, 33.1, 22.3, 13.9 ppm. *GC-MS*: *m/z* (%) = 318 [M^+], 161 (100), 91 (30).

*Se-phenyl 3,5-dinitrobenzoselenoate (**2d**)*: ^{1}*H-NMR* ($CDCl_3$, 200 MHz): δ = 9.28 (t, J = 2.05 Hz, 1H, H-Ar), 9.04 (d, J = 2.06 Hz, 2H, H-Ar), 7.7–7.4 (m, 5H, H-Ar) ppm. ^{13}*C-NMR* ($CDCl_3$, 50 MHz): δ = 190.4, 148.9, 141.5, 136.1, 130.07, 129.9, 126.7, 124.1, 122.6 ppm.

*Se-phenyl thiophene-2-carboselenoate (**2e**)*: pale oil; ^{1}*H-NMR* ($CDCl_3$, 200 MHz): δ = 7.88 (dd, J = 1.2, 3.9 Hz, 1H, H-Ar), 7.71 (dd, J = 1.2, 4.96 Hz, 1H, H-Ar), 7.63–7.58 (m, 2H, H-Ar), 7.44–7.41 (m, 3H, H-Ar), 7.17 (dd, J = 3.9, 4.96 Hz, 1H, H-Ar) ppm. ^{13}*C-NMR* ($CDCl_3$, 50 MHz): δ = 183.6, 143.1, 136.3, 133.7, 132.0, 129.4, 129.2, 128.0, 125.5 ppm. *GC-MS*: *m/z* (%) = 268 (1) [M^+], 157 (16), 111 (100), 83 (20).

*(E)-Se-phenyl 3-phenylprop-2-eneselenoate (**2f**)*: ^{1}*H-NMR* ($CDCl_3$, 200 MHz): δ = 7.58–7.54 (m, 5H, H-Ar), 7.43–7.40 (m, 6H, H-Ar), 6.78 (d, J = 15 Hz, 1H, CH) ppm. ^{13}*C-NMR* ($CDCl_3$, 50 MHz): δ = 190.8, 141.1, 135.9, 133.9, 130.9, 129.4, 129.1, 129.0, 128.6, 128.1, 126.3 ppm. *GC-MS*: *m/z* (%) = 288 (1) [M^+], 157 (14), 131 (100), 103 (55), 77 (36).

*Se-phenyl 2-phenylethaneselenoate (**2g**)*: ^{1}*H-NMR* ($CDCl_3$, 200 MHz): δ = 7.45–7.35 (m, 2H, H-Ar), 7.34–7.26 (m, 8H, H-Ar), 3.88 (s, 2H, CH_2) ppm. ^{13}*C-NMR* ($CDCl_3$, 50 MHz): δ = 198.9, 135.8, 132.6, 130.1, 129.3, 128.9, 128.8, 127.8, 126.6, 53.6 ppm. *GC-MS*: *m/z* (%) = 276 (10) [M^+], 157 (22), 119 (26), 91 (100), 65 (26).

*4-(Phenylselanyl)butyl benzoate (**5a**)*: pale oil; ^{1}*H-NMR* ($CDCl_3$, 200 MHz): δ = 7.99–7.94 (m, 2H, H-Ar), 7.48–7.35 (m, 5H, H-Ar), 7.21–7.18 (m, 3H, H-Ar), 4.27 (t, J = 5.5 Hz, 2H, CH_2-O), 2.92 (t, J = 6.3 Hz, 2H, CH_2-Se), 1.90–1.78 (m, 4H, CH_2) ppm. ^{13}*C-NMR* ($CDCl_3$, 50 MHz): δ = 166.5, 132.8, 132.6, 130.2, 129.9, 129.5, 128.9, 128.3, 126.8, 64.2, 28.7, 27.3, 26.6 ppm.

*4-(Phenylselanyl)butyl 2-bromobenzoate (**5b**)*: pale oil; ^{1}*H-NMR* ($CDCl_3$, 200 MHz): δ = 7.69 (m, 2H, H-Ar), 7.49 (m, 2H, H-Ar), 7.35–7.22 (m, 5H, H-Ar), 4.33 (t, J = 5.7 Hz, 2H, CH_2-O), 2.96 (t, J = 6.7 Hz, 2H, CH_2-Se), 1.9–1.85 (m, 4H, CH_2) ppm. ^{13}*C-NMR* ($CDCl_3$, 100 MHz): δ = 166.2, 134.3, 132.7, 132.5, 132.4, 131.2, 130.0, 129.1, 127.1, 126.9, 121.6, 64.9, 28.6, 27.3, 26.7 ppm.

*4-(Phenylselanyl)butyl 4-butylbenzoate (**5c**)*: pale oil; ^{1}*H-NMR* ($CDCl_3$, 200 MHz): δ = 7.9 (d, J = 8.03, 2H, H-Ar), 7.5–7.47 (m, 2H, H-Ar), 7.25–7.22 (m, 5H, H-Ar), 4.3 (t, 2H, CH_2O), 2.96 (t, 2H, CH_2Se), 2.66 (t, J = 8 Hz, 2H, CH_2), 1.94–1.87 (m, 4H, CH_2), 1.61–1.53 (m, 2H, CH_2), 1.37–1.30 (m, 2H, CH_2), 0.93 (t, J = 7.16 Hz, 3H, CH_3) ppm. ^{13}*C-NMR* ($CDCl_3$, 100 MHz): δ = 166.6, 148.5, 132.7, 130.1, 129.6, 129.0, 128.5, 127.7, 126.8, 64.06, 35.7, 33.3, 28.8, 27.4, 26.2, 22.3, 13.9 ppm.

*4-(Phenylselanyl)butyl thiophene-2-carboxylate (**5e**)*: pale oil; ^{1}*H-NMR* ($CDCl_3$, 200 MHz): δ = 7.76 (dd, J = 1.18, 3.72 Hz, 1H, H-Ar), 7.56–7.47 (m, 3H, H-Ar), 7.25–7.22 (m, 3H, H-Ar), 7.09 (dd, J = 3.78, 4.96 Hz, 1H, H-Ar), 4.29 (t, J = 6 Hz, 2H, CH_2), 2.96 (t, J = 6.7 Hz, 2H, CH_2), 1.92–1.80 (m, 4H, CH_2) ppm. ^{13}*C-NMR* ($CDCl_3$, 100 MHz): δ = 162.2, 133.8, 133.3, 132.7, 132.3, 130.0, 129.05, 127.7, 126.8, 64.5, 28.7, 27.3, 26.6 ppm.

*4-(Phenylselanyl)butyl 2-phenylacetate (**5g**)*: pale oil; ^{1}*H-NMR* ($CDCl_3$, 200 MHz): δ = 7.5–7.45 (m, 2H, H-Ar), 7.37–7.23 (m, 8H, H-Ar), 4.09 (t, J = 6.1 Hz, 2H, CH_2O), 3.6 (s, 2H, CH_2), 2.89 (t, J = 6.9 Hz, 2H, CH_2Se), 1.8–1.7 (m, 4H, CH_2) ppm. ^{13}*C-NMR* ($CDCl_3$, 100 MHz): δ = 171.6, 134.03, 132.7, 130.1, 129.25, 129.1, 128.6, 127.1, 126.9, 64.25, 41.4, 28.6, 27.3, 26.5 ppm.

*4-(4-(Phenylselanyl)butoxy)butyl benzoate (**6a**)*: pale oil; ^{1}*H-NMR* ($CDCl_3$, 200 MHz): δ = 8.07–8.02 (m, 2H, H-Ar), 7.56–7.4 (m, 5H, H-Ar), 7.26–7.22 (m, 3H, H-Ar), 4.33 (t, J = 6.38 Hz, 2H, CH_2O), 3.93 (dt, J_d = 6.02 Hz, J_t = 6.2 Hz, 4H, CH_2), 2.93 (t, J = 7.1 Hz, 2H, CH_2Se), 1.86–1.67 (m, 8H, CH_2) ppm. ^{13}*C-NMR* ($CDCl_3$, 50 MHz): δ = 166.6, 132.9, 132.45, 130.45, 130.4, 129.5, 129.0, 128.3, 126.7, 70.2, 64.8, 29.8, 27.7, 26.9, 26.4, 25.6 ppm.

*4-(4-(Phenylselanyl)butoxy)butyl 2-bromobenzoate (**6b**)*: pale oil; ^{1}*H-NMR* ($CDCl_3$, 200 MHz): δ = 7.8–7.63 (m, 2H, H-Ar), 7.5–7.22 (m, 7H, H-Ar), 4.35 (t, J = 6.29 Hz, 2H, CH_2O), 3.42 (dt, J_d = 5.7 Hz, J_t = 6.18 Hz, 4H, CH_2), 2.92 (t, J = 7.2 Hz, 2H, CH_2Se), 1.84–1.67 (m, 8H, CH_2) ppm. *[13]C-NMR* ($CDCl_3$, 100 MHz): δ = 166.3, 134.3, 132.5, 132.4, 132.37, 131.2, 128.9, 127.1, 126.7, 121.5, 70.2, 70.16, 65.5, 29.8, 27.7, 26.9, 26.3, 25.5 ppm.

*4-(4-(Phenylselanyl)butoxy)butyl thiophene-2-carboxylate (**6e**):* pale oil; *[1]H-NMR* ($CDCl_3$, 200 MHz): δ = 7.79 (dd, J = 1.2, 3.7 Hz, 1H, H-Ar), 7.55 (m, 3H, H-Ar), 7.26 (m, 3H, H-Ar), 7.09 (dd, J = 3.74, 4.98 Hz, 1H, H-Ar), 4.3 (t, J = 6.25, 2H, CH_2O), 3.42 (dt, J_d = 5.29 Hz, J_t = 6.2 Hz, 4H, CH_2), 2.92 (t, J = 7.1 Hz, 2H, CH_2Se), 1.83–1.65 (m, 8H, CH_2) ppm. *[13]C-NMR* ($CDCl_3$, 100 MHz): δ = 162.3, 133.9, 133.3, 132.5, 132.2, 130.4, 129.1, 128.9, 127.7, 126.7, 70.2, 64.9, 29.8, 29.7, 27.7, 26.9, 26.3, 25.6 ppm.

*4-(4-(Phenylselanyl)butoxy)butyl 2-phenylacetate (**6g**):* pale oil; *[1]H-NMR* ($CDCl_3$, 200 MHz): δ = 7.51–7.47 (m, 2H, H-Ar), 7.33–7.24 (m, 8H, H-Ar), 4.1 (t, J = 6.05 Hz, 2H, CH_2O), 3.62 (s, 2H, CH_2), 3.38 (dt, J_d = 2.3 Hz, J_t = 6.1 Hz, 4H, CH_2), 2.93 (t, J = 6.8 Hz, 2H, CH_2Se), 1.8–1.55 (m, 8H, CH_2) ppm. *[13]C-NMR* ($CDCl_3$, 100 MHz): δ = 172.0, 134.1, 132.5, 130.5, 129.25, 129, 128.5, 127.05, 126.7, 70.2, 64.7, 41.5, 28.8, 27.7, 26.9, 26.2, 25.5 ppm.

3. Results and Discussion

After the zinc mediated reduction of diphenyl diselenide in the biphasic system composed by a 1 : 1 mixture of 10% aq. HCl and diethyl ether (2 mL), 1 equivalent of the acyl chloride **1a**–**g** was added and the mixture was stirred in a closed vial for 4 h. The results reported in Table 1 evidenced that the nucleophilic acyl substitution proceeded in moderated to good yields only in the case of aryl carboxylic derivatives **1a**-**c** and **1e** and not in the case of vinyl (**1f**) or alkyl (**1g**) analogues. Starting from substrates bearing functional group susceptible to reductive conditions (**1d**), a complex mixture of unidentified compounds was obtained.

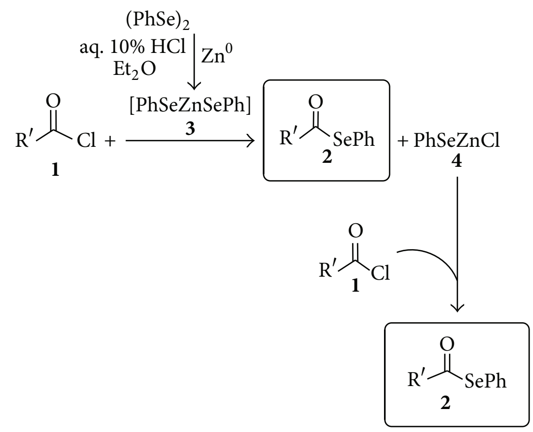
The proposed mechanism for the reaction is reported in Scheme 3. The zinc-selenolate **3**, originated by reduction of diphenyl diselenide, attacks the carbonyl group promoting the nucleophilic substitution of the chloro atom. From this reaction, the formation of a molecule of PhSeZnCl **4** can be speculated. This reagent has been proven to be an effective nucleophile for the synthesis of selenoesters in "on water conditions" [17].

With the only exception of **1d**, in all the cases the only side product observed was the carboxylic acid, indicating that the hydrolysis strongly competes with the desired reaction. With the aim to improve the yield of selenoesters **3** using in the reaction model benzoyl chloride **1a**, we changed the conditions generating the selenium-zinc complex in THF under the catalysis of trifluoromethanesulfonic acid (TfOH) as anhydrous acid (Table 2, entry **1**). After the formation of the selenolate, which occurs during time t_1, benzoyl chloride **1a** was added and stirred for the additional time t_2. The entire reaction was performed at the same temperature indicated in Table 2.

Surprisingly, beside the desired product, we observed the formation of side compounds in which the carboxylic moiety

Table 2: Preliminary results (see Scheme 4).

Entry	mol% of acid	t_1	t_2	T	Ratios by [1]H-NMR 2a	5a	6a
1	60	1 h	3 h	rt	26	48	26
2	30	1 h	3 h	rt	38	34	28
3	60	1 h	1 h 30′	Reflux	36	38	26
4	30	1 h	1 h 30′	Reflux	32	42	26
5	30	6 h	1 h 30′	Reflux	42	38	20



Scheme 3

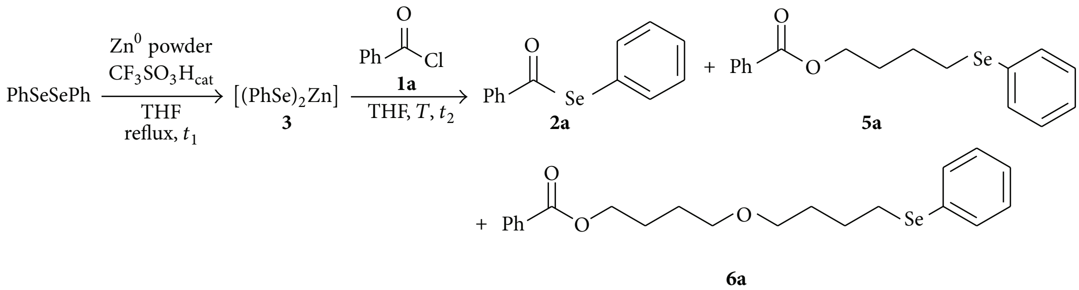
and the selenium are spaced by one (**5a**) or two (**6a**) 4-carbon units deriving from the ring opening of THF (Scheme 4). Changes on the acid amount, the t_2, as well as the reaction temperature T, did not produce evident effect on the ratios between selenoester **2a** and the side products **5a** and **6a** (Table 2, entries **1**–**4**).

Interestingly, also a strong increment of t_1 (from 1 h to 6 h) did not produce effect on the products ratio, clearly indicating that the ring-opening process did not occur during this time but it is, reasonably, a concerted mechanism that involves both the selenium nucleophile **3** and the electrophilic **1a**.

Using the best reaction conditions reported in Table 2, entry **4**, we explored the reactivity of acyl chlorides **1a**–**g** and the results are summarized in Table 3.

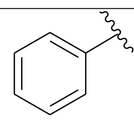
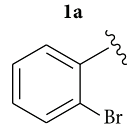
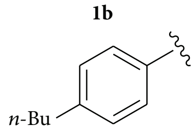
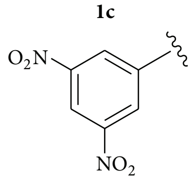
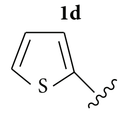
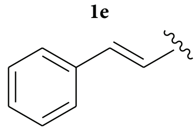
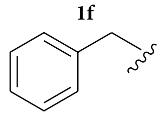
In all the cases, the ratios were calculated by [1]H-NMR of the crude. Yields are referred to the overall isolated products after purification by flash chromatography. All the structures were assigned based on [1]H-NMR and [13]C-NMR analysis.

In some cases, (Table 3, entries **1**, **3**, **5**, and **7**), both side products (**5** and **6**) were observed in a comparable amount with respect to the selenol ester **2**. In the case of the electron rich acyl chloride **1c**, the yield of selenol ester **2c** was lower (34%) and only **5c** was formed as side product. Interestingly, the reaction from the strongly electrophilic **1d** afforded quantitatively the target compound **2d**. The chloride of the cinnamic acid **1f** confirmed a scarce reactivity affording **2f** only in 20% yield associated with the chlorine derivative **7f** (Scheme 5).



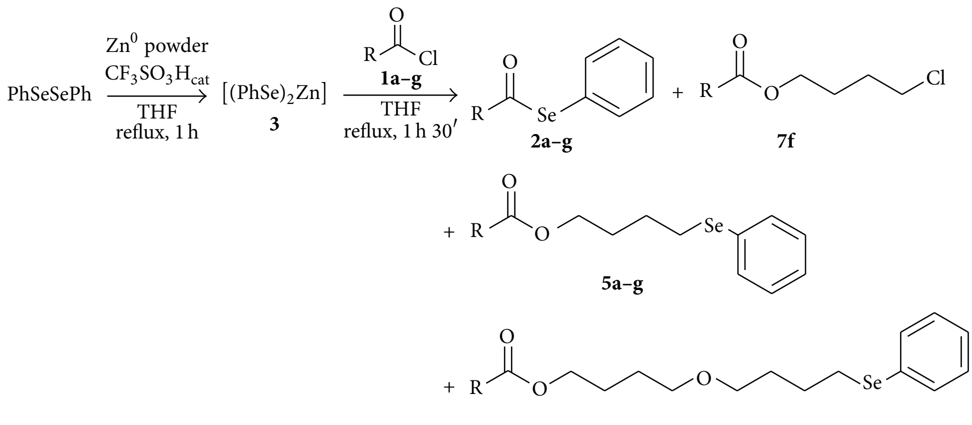
Scheme 4

Table 3: Scope of the reaction in THF (see Scheme 5).

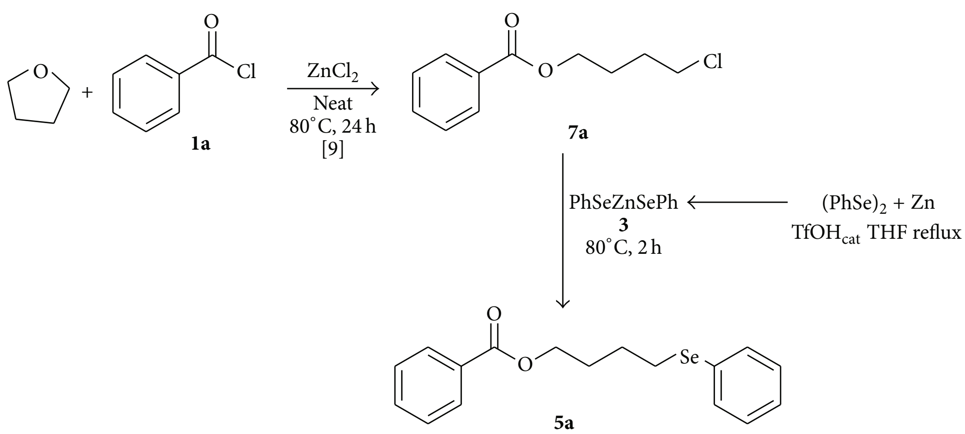
Entry	R	Yield	Ratio			
			2	**5**	**6**	**7**
1	 **1a**	60%	32	42	26	—
2	 Br **1b**	60%	63	23	14	—
3	 n-Bu **1c**	50%	68	32	—	—
4	 O_2N NO_2 **1d**	100%	100	—	—	—
5	 S **1e**	64%	34	47	19	—
6	 **1f**	24%	83	—	—	7
7	 **1g**	78%	80	15	5	—

In order to verify if chloride intermediate **7** is involved in the formation of **5** and **6** or if it is formed through a parallel mechanism based on the nucleophilicity of the chloride anion, **7a** was prepared according to the procedure reported by Enthaler and Weidauer [18] reacting benzoyl chloride **1a** and $ZnCl_2$ in THF (Scheme 6).

After isolation of **7a**, it was reacted with a preformed suspension of **3**, following the condition reported in Table 2, entry **4,** for the second part of the reaction (time t_2). The NMR analysis of the crude evidenced the formation of **5a** only in traces, confirming that, in the principal mechanism, chloride **7** is not the precursor of products **5** and **6**.



Scheme 5



Scheme 6

All these evidences suggested a concerted mechanism in which three parallel reactions can be envisioned.

Zinc-selenolate complexes **3** or **4** can attack directly acyl chloride affording the selenoesters **2** (black path in Scheme 7). Alternatively, the same complexes, which reasonably in THF solution coordinate one or two molecules of solvent, attack the carbon of THF and the nucleophilic oxygen can be immediately quenched by the electrophile **1**, affording **5** (red path in Scheme 7), or open a second molecule of THF and then react with acyl chloride **1** to afford **6** (green path in Scheme 7). From the PhSeZnCl **4,** a similar mechanism can be activated by the chloride, producing the ester **7** (blue path in Scheme 7).

4. Conclusions

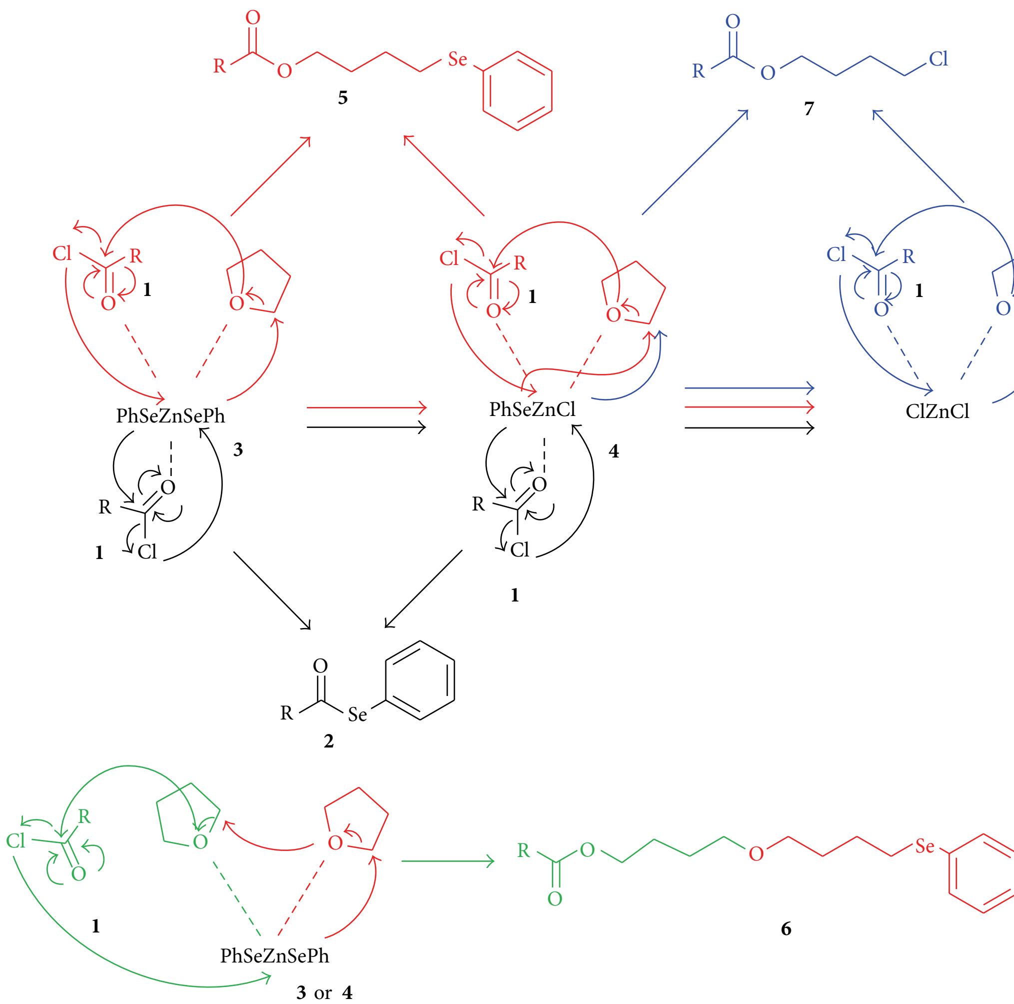
In conclusion, we demonstrated that aqueous or anhydrous acidic conditions can be used to activate the zinc mediated reduction of diphenyl diselenide. The corresponding zinc-selenolate complex has been studied toward the reaction with a series of acyl chloride affording the corresponding selenol esters in moderate to good yields depending on the substrate and the reaction conditions. The presence of zinc and the strong hydrolytic conditions limit the scope of the reaction. Performing the reaction in refluxing THF, the ring-opening reaction of the solvent competes with the acyl substitution and it was not possible to find conditions to improve the selectivity of the process. Nevertheless, the reaction in THF resulted in being effective for some substrates that failed in the biphasic system (**1d**, **1f**, and **1g**). In addition, the possibility of using this process to depolymerize polyether based materials is an attracting and promising prospective that is currently under investigation exploring the possibility of transforming wastes in highly functionalized selenium containing chemicals.

Competing Interests

The authors declare that there is no conflict of interests.

Authors' Contributions

Gemma Bellino and Marialaura Scisciani contributed equally to this work.



Scheme 7

Acknowledgments

Financial support from the Dipartimento di Scienze Farmaceutiche, Università degli Studi di Perugia "Fondo per il sostegno della Ricerca di Base 2015," and Fondazione Cassa di Risparmio di Perugia (2014.01000.021) are acknowledged. The authors thank Regione Umbria, project "POR Umbria 2007–2013," for the fellowship to Luca Sancineto. Eder Joao Lenardao is Bolsista CAPES—Processo no. BEX 6391/14-1 and Mrs. Vargas was in CAPES Sandwich program with a Doctorate scholarship (PDSE process 99999.001342/2014-02). This research was undertaken as part of the scientific activity of the international multidisciplinary "SeS Redox and Catalysis" network.

References

[1] T. Wirth, Ed., *Organoselenium Chemistry—Synthesis and Reactions*, Wiley-VCH, Weinheim, Germany, 2011.

[2] S. Santoro, J. B. Azeredo, V. Nascimento, L. Sancineto, A. L. Braga, and C. Santi, "The green side of the moon: ecofriendly aspects of organoselenium chemistry," *RSC Advances*, vol. 4, no. 60, pp. 31521–31535, 2014.

[3] C. Santi, C. Tidei, C. Scalera, M. Piroddi, and F. Galli, "Selenium containing compounds from poison to drug candidates: a review on the GPx-like activity," *Current Chemical Biology*, vol. 7, no. 1, pp. 25–36, 2013.

[4] A. Pacula, F. Mangiavacchi, L. Sancineto, E. J. Lenardao, J. Ścianowski, and C. Santi, "An Update on 'selenium containing compounds from poison to drug candidates: a review on the GPx-like activity'," *Current Chemical Biology*, vol. 9, no. 2, pp. 97–112, 2016.

[5] J.-C. Wu and J. Chattopadhyaya, "Michael addition reactions of $\alpha\beta$-ene-3′-phenylselenone of uridine. New synthesis of 2′,3′-dideoxy-ribo-aziridino-, 2′,3′-dideoxy-2′, 3′-ribo-cyclopropyl- & 2,2′-*O*-anhydro-3′-deoxy-3′-amino uridine derivatives," *Tetrahedron*, vol. 45, no. 14, pp. 4507–4522, 1989.

[6] D. Crich and D. Grant, "Synthesis of a 4,6-disubstituted dibenzofuran β-sheet initiator by reductive radical arylation of benzene," *Journal of Organic Chemistry*, vol. 70, no. 6, pp. 2384–2386, 2005.

[7] T. R. Hoye and A. J. Caruso, "A 1,3-diene-2-carboxylic ester synthesis; reaction of alkylidene-γ-lactones with potassium and sodium phenyl selenoate," *Tetrahedron Letters*, vol. 19, no. 47, pp. 4611–4614, 1978.

[8] D. Liotta, U. Sunay, H. Santiesteban, and W. Markiewicz, "Phenyl selenide anion, a superior reagent for the SN2 cleavage of esters and lactones," *Journal of Organic Chemistry*, vol. 46, no. 13, pp. 2605–2610, 1981.

[9] S. M. Salman, R. S. Schwab, E. E. Alberto et al., "Efficient ring opening of protected and unprotected aziridines promoted by stable zinc selenolate in ionic liquid," *Synlett*, no. 1, Article ID S07210ST, pp. 69–72, 2011.

[10] C. Santi, S. Santoro, L. Testaferri, and M. Tiecco, "A simple zinc-mediated preparation of selenols," *Synlett*, no. 10, pp. 1471–1474, 2008.

[11] C. Tidei, L. Sancineto, L. Bagnoli, B. Battistelli, F. Marini, and C. Santi, "A recyclable biphasic system for stereoselective and easily handled hydrochalcogenations," *European Journal of Organic Chemistry*, vol. 2014, no. 27, pp. 5968–5975, 2014.

[12] P. Dreyfuss, M. P. Dreyfuss, and G. Pruckmayr, *Encyclopedia of Polymer Science and Engineering*, vol. 16, John Wiley & Sons, New York, NY, USA, 2nd edition, 1989.

[13] S. Penczek, P. Kubisa, and K. Matyjaszewski, "Introduction," in *Cationic Ring-Opening Polymerization of Heterocyclic Monomers*, vol. 37 of *Advances in Polymer Science*, pp. 1–2, 1980.

[14] A. Rosowski, "Ethylene oxide," in *Heterocyclic Compounds with Three and Four Membered Rings, Part 1*, A. Weissberger, Ed., Interscience, New York, NY, USA, 1964.

[15] S. Kobayashi, M. Sugiura, H. Kitagawa, and W. W.-L. Lam, "Rare-earth metal triflates in organic synthesis," *Chemical Reviews*, vol. 102, no. 6, pp. 2227–2302, 2002.

[16] A. Kudelko and M. Wróblowska, "An efficient synthesis of conjugated 5-aryl-1,3,4-oxadiazoles from 3-heteroarylacrylohydrazides and acid chlorides," *Tetrahedron Letters*, vol. 55, no. 21, pp. 3252–3254, 2014.

[17] C. Santi, B. Battistelli, L. Testaferri, and M. Tiecco, "On water preparation of phenylselenoesters," *Green Chemistry*, vol. 14, no. 5, pp. 1277–1280, 2012.

[18] S. Enthaler and M. Weidauer, "Zinc-catalyzed depolymerization of artificial polyethers," *Chemistry—A European Journal*, vol. 18, no. 7, pp. 1910–1913, 2012.