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Rongalite®/PEG-400 as reducing system in the synthesis of new glycerol-derived selenol esters using anhydrides and bis-(2,2-dimethyl-1,3-dioxolanylmethyl)diselenide as substrates

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Dedicated to Professor Jacek Młochowski on the occasion of his 80th anniversary

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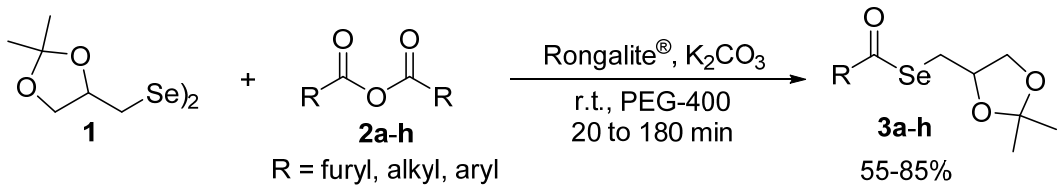
Abstract

A green method for the synthesis of new glycerol-derived selenol esters was developed by reactions between several anhydrides and bis-(2,2-dimethyl-1,3-dioxolanylmethyl)diselenide using Rongalite®, K_2CO_3 and polyethylene glycol-400 (PEG-400) as the solvent. These reactions were efficiently conducted under mild conditions, employing stable and non-hazardous starting materials and in short reaction times (20-180 min), affording the corresponding selenol esters in moderate to good yields (55-85%) at room temperature. Further, it was demonstrated that deprotection of the ketal protecting group of the selenol ester **3**, with acidic cation-exchange resin Dowex®50WX8, produces the water-soluble selenol ester.



Keywords: PEG-400, glycerol, selenol esters, Rongalite®, organochalcogen compounds

Introduction

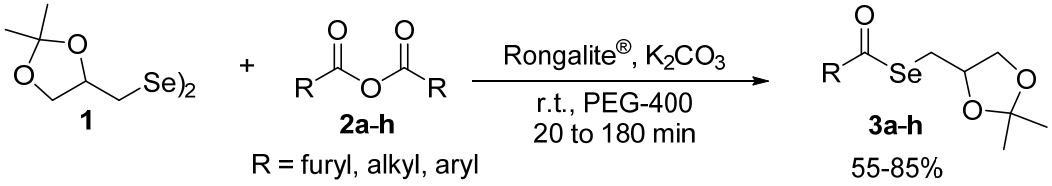
Selenol esters are important intermediates in organic synthesis, as well as have interesting biological activities. They have been used as precursors of acyl radicals and anions,[1-4] intermediates in the synthesis of ketones,[5,6] as building blocks of heterocyclic compounds,[7] in Diels–Alder,[8,9] cyclocondensation[10] and various cyclization reactions.[11-14] They were also used as a precursors in the synthesis of vinyl compounds,[15] in the formation of C-peptide bonds,[16-18] and the synthesis of some natural occurring compounds,[19-23] besides having proven antioxidant properties.[24]

Various methods have been described for the synthesis of selenol esters, for example, by the condensation of selenolate anions[25] or radicals[26] with carbonyl compounds, such as aldehydes,[27,28] anhydrides[26,29-34] acyl chlorides[29-34] or starting from chalcogen acetylenes[35] and aryl iodides.[36] Generally, these methods have limitations related to metal-catalyzed synthesis,[37] high temperatures and volatile solvents[29] and long reaction times.[32] However, new methods have been described to meet the principles of green chemistry, for instance, by using alternative and recyclable solvents,[25,38] microwave irradiation,[39] solvent-free and metal-free conditions.[27]

In recent years, the importance of sustainable chemistry for the preparation of chalcogen-containing compounds (S, Se and Te) has increased.[40] In this context, polyethylene glycol (PEG-400) is considered to be a green solvent because it has negligible vapor pressure, is biodegradable, biocompatible, non-toxic, non-volatile and has a low flammability.[41]

Glycerol has emerged in the recent years as both a solvent and a reagent for green chemistry. In this sense, five-membered cyclic ketals, which are synthesized by the reaction of the terminal and central hydroxyl groups of the glycerol with a ketone, have many applications, especially their use as an additive for fuels and solvents, and as intermediates in pharmaceutical industry.[42] In recent years, our group have reported new derivatizations of such ketals, including the preparation of chalcogen-containing analogs of solketal, like 4-thiomethyl-1,3-dioxolan-2-ones,[43] vinyl- or alkynyl chalcogenides[44] and enantiomerically pure bis-(2,2-dimethyl-1,3-dioxolanylmethyl)chalcogenides and dichalcogenides.[45]

As a continuation of our studies on the utilization of the glycerol-derivative bis-(2,2-dimethyl-1,3-dioxolanylmethyl)diselenide[44] **1** in organic synthesis, we present here our results on the reaction of diselenide **1** with anhydrides **2a-h** for the synthesis of selenol esters **3a**-**h** by a clean method, using Rongalite® (sodium hydroxymethanesulfinate dihydrate, $HOCH_2SO_2Na$)[46] in the presence of a base and using PEG-400 as green solvent (Scheme 1).

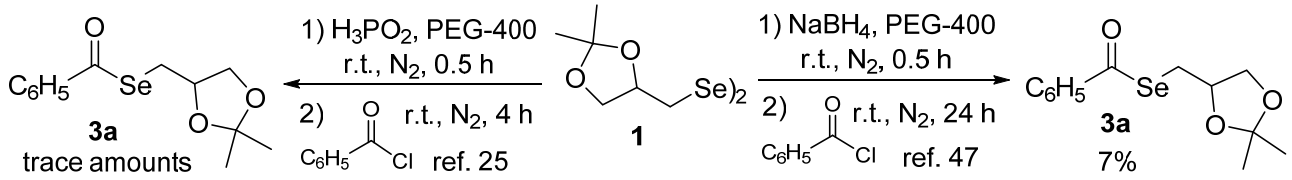


Scheme 1. Synthesis of selenol esters **3a**-**h**.

Results and Discussion

Our initial efforts were directed at combining our interest in the synthesis of glycerol derivatives containing an organochalcogen unit with the development of eco-friendly reductive systems for the synthesis of selenol

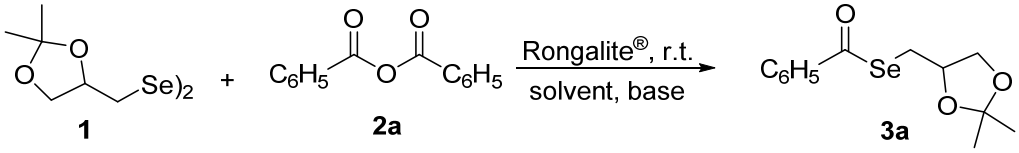
esters, described by us in 2015,[25] which involves the use of the polyethylene glycol-400/H_3PO_2 system to cleave the Se-Se bond (Scheme 2). Unfortunately, the reaction between bis-(2,2-dimethyl-1,3-dioxolanylmethyl)diselenide **1** and benzoyl chloride did not work well, probably due the various reactive centers in an acidic medium. After that, we tried the reaction using the polyethylene glycol-400/$NaBH_4$ system, which was successful for the generation of selenolate and tellurolate anions *in situ*.[47] However, the desired selenol ester was obtained in only 7% yield (Scheme 2).



Scheme 2. Synthesis of selenol ester **3a** from benzoyl chloride and diselenide **1**.

Another convenient methodology to prepare selenol esters involves the use of Rongalite® in basic medium to generate the nucleophilic selenium species *in situ*, that then undergoes acylation with anhydrides. Inspired by the results of Dan and co-workers,[26] we decided to apply their conditions to the reaction of our substrate **1** (1.0 mmol) with benzoic anhydride **2a** (1.1 mmol), in the presence of K_2CO_3 (1.0 mmol), Rongalite® (1.5 mmol) and DMF as the solvent. Under these conditions, the desired product **3a** was obtained in 66% yield after only 20 min of reaction in a sealed vial (Table 1, entry 1). In order to optimize the above protocol to establish the best conditions for the reaction, several experiments, including the use of other bases and solvents, were performed to synthesize the selenol ester **3a** (Table 1).

Table 1. Optimization of the synthesis of selenol ester **3a**[a]



Entry	Base	Time (min)	Solvent	Yield (%)[b]
1	K_2CO_3	20	DMF	66
2	Cs_2CO_3	20	DMF	56
3	CsF	20	DMF	45
4	K_2CO_3	20	PEG-400	70
5	Cs_2CO_3	20	PEG-400	64
6	CsF	180	PEG-400	42
7	$NaHCO_3$	60	PEG-400	57
8	Na_2CO_3	360	PEG-400	36

[a] The reactions were performed using bis-(2,2-dimethyl-1,3-dioxolanylmethyl)diselenide **1** (0.5 mmol), benzoic anhydride **2a** (1.1 mmol), base (0.5 mmol), Rongalite® (1.5 mmol) and solvent (3.0 mL) at room temperature. [b] Yields are given for isolated product **3a**.

A comparative study was carried out using different bases and solvents (Table1, entries 1 to 6) and to our gratification, PEG-400 proved to be a better solvent than DMF for this reaction by using cesium or potassium carbonate, giving the product **3a** in 64% and 70% yields, respectively. Interestingly, selenol ester **3a** was formed in only 42% and 45% yields when cesium fluoride, the base originally used by Dan and co-workers, was present (Table 1, entries 3 and 6). Furthermore, other bases such as sodium bicarbonate and carbonate were also evaluated, with the product being obtained in 57% and 36% yields, respectively (Table 1, entries 7 and 8).

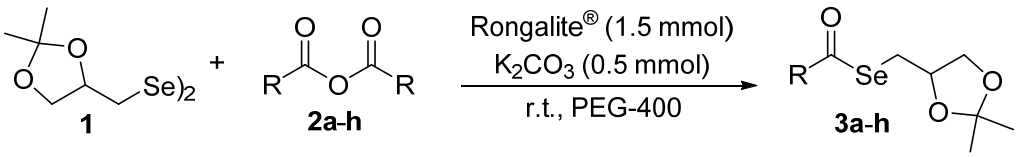
Thus, analyzing the results shown in Table 1, we established the best reaction conditions as those in the previous reaction of bis-(2,2-dimethyl-1,3-dioxolanylmethyl)diselenide **1** (0.5 mmol) and anhydride **2** (1.1 mmol) in the presence of K_2CO_3 (1.0 mmol), Rongalite® (1.5 mmol), PEG-400 (3.0 mL) in a sealed vial at room temperature.

In order to demonstrate the efficiency and generality of this protocol, we attempted to extend the method using anhydrides with different substitution patterns (**2b-h**) as substrates in the reaction with diselenide **1**. Inspection of the results in Table 2 reveals that the Rongalite®/PEG-400-based protocol worked well for a range of substrates, giving products **3a**-**h** in moderate to good yields. First of all, we described the synthesis of (*S*)- and (*R*)-Se-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]benzoselenoate **3a**, starting from the respective enantiomerically pure (*S*,*S*)- and (*R*,*R*)-diselenide[45] **1** (Table 2, entries 2-3).

Next, a range of aromatic anhydrides containing electron-withdrawing (EWG) as well as electron-donating groups (EDG) **2b**-**e** were reacted with diselenide **1**, to give the respective selenol esters **3b**-**e**. Whereas the reaction of unsubstituted aromatic anhydride **2a** was complete in just 20 min, the presence of an EDG or EWG in the aromatic ring of **2**, caused an increase in the reaction time to 40 to 80 min (Table 4, entries 4-7). Despite the decrease in the reactivity, it seems that the reactions are somewhat sensitive to electronic effects due to the substituents in the *para* position. For example, 4-methylbenzoic anhydride **2b** gave a slightly higher yield than 4-Br (**2c**) and 4-Cl (**2d**) and even unsubstituted **2a** (Table 2, entries 1 and 4-6). Interestingly, when the 2-Cl substituted anhydride **2e** was used, the reaction was slower and the product **3e** was isolated in 85% yield after 80 min (Table 2, entry 7).

The reaction performed with the heteroaromatic 2-furyl anhydride **2f** furnished the respective product **3f** in moderate yield (70%) after 180 min (Table 2, entry 8). Good results were obtained also with aliphatic acetic anhydride **2g** and pivalic anhydride **2h** and the corresponding selenol esters **3g** and **3h** were obtained in 70 and 72% yields, respectively, after 180 and 120 min of reaction (Table 2, entries 9-10).

Table 2. Synthesis of selenol esters **3** by acylation of diselenides **1**[a]



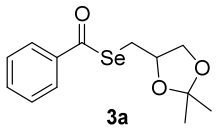
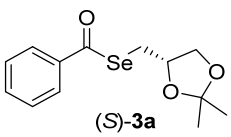
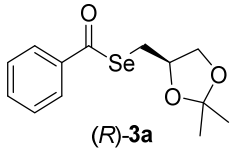
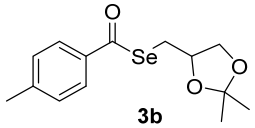
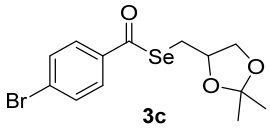
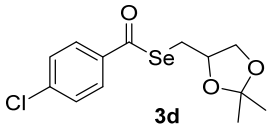
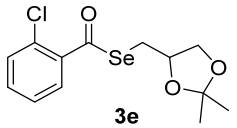
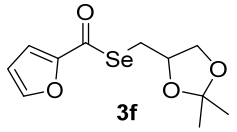
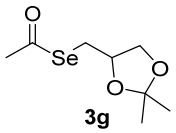
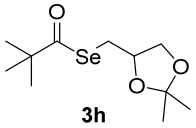
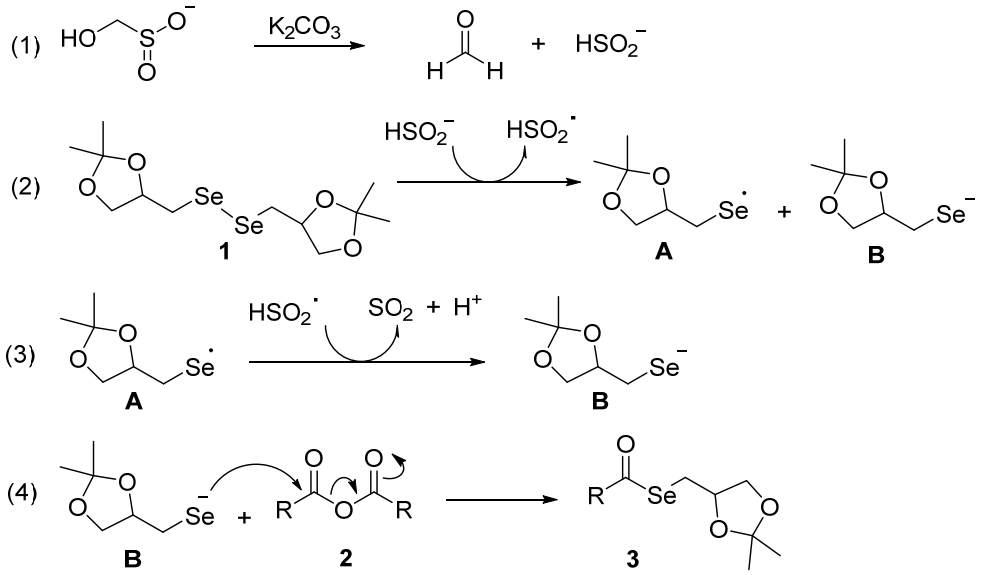
Entry	Product **3**	Time (min)	Yield (%)[b]
1	 **3a**	20	70
2	 (*S*)-**3a**	20	75

Table 2. Continued

Entry	Product **3**	Time (min)	Yield (%)[b]
3	 (*R*)-**3a**	20	66
4	 **3b**	60	81
5	 **3c**	60	71
6	 **3d**	40	55
7	 **3e**	80	85
8	 **3f**	180	70
9[c]	 **3g**	180	70
10	 **3h**	120	72

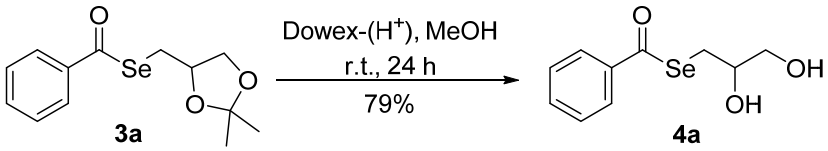
[a] The reactions were performed in the presence of bis-(2,2-dimethyl-1,3-dioxolanylmethyl)diselenide **1** (0.5 mmol), anhydride **2a**-**h** (1.1 mmol), K_2CO_3 (0.5 mmol), Rongalite® (1.5 mmol) and PEG-400 (3.0 mL) at room temperature. [b] Yields are given for isolated product **3a**-**h**. [c] Reaction performed with 1.5 mmol of anhydride **2g**.

According to the previously proposed mechanism of the reduction of a dichalcogenide by Rongalite®,[26,48,49] a plausible mechanism for the formation of selenol esters **3** is showed in Scheme 3. Firstly, Rongalite® when treated with K_2CO_3 decomposes to formaldehyde and HSO_2^- (*step 1*), which transfers a single electron to the diselenide **1**, resulting in the formation of two radical intermediates $HSO_2^{\bullet}$ and **A**, and the selenolate anion **B** (*step 2*). The selenium radical **A** is further reduced to the anionic species **B**, by another single electron transfer (*step 3*). Finally, nucleophilic attack of intermediate **B** on the carbonyl carbon atom would form the desired selenol ester **3**, along with carboxylic acid (*step 4*).



Scheme 3. Plausible mechanism for the formation of selenol esters **3**.

Once we had prepared a series of selenol esters derivative of glycerol, we evaluated the deprotection reaction of the ketal **3a**, aiming to prepare the water-soluble selenol ester **4a**. Thus, stirring a solution of **3a** in methanol at room temperature with a solid acid for 24 h afforded *Se*-(2,3-dihydroxypropyl)benzoselenoate **4a** in 79% yield (Scheme 4).[50] The solubility of the selenol ester **4a** was determined as 8.6 g/mL at room temperature.



Scheme 4. Synthesis of *Se*-(2,3-dihydroxypropyl)benzoselenoate **4a**.

Conclusion

We have demonstrated here the efficient synthesis of new glycerol-based selenol esters by a green method using PEG-400 as the solvent and Rongalite® as an inexpensive reducing agent for the cleavage of the Se-Se bond. This method involves reactions of aromatic, aliphatic and heteroaromatic anhydrides **2** with racemic and enantiomerically pure bis-(2,2-dimethyl-1,3-dioxolanylmethyl)diselenide **1** at room temperature under basic medium. In this work, the products were prepared in moderate to good yields (55-85%) after 20-180 min of reaction. Additionally, it was demonstrated that the deprotection of the ketal protecting group in the selenol ester **3** produces water-soluble selenol ester, which could be tested for its pharmacological activities.

Experimental Section

General. The reactions were monitored by thin layer chromatography (TLC) which was performed using Merck silica gel (60 F_{254}), 0.25 mm thickness. For visualizing the spots, TLC plates were either exposed to UV light, or stained with iodine vapor, or 5% vanillin in 10% H_2SO_4 and heat. Column chromatography was performed using Merck Silica Gel (230-400 mesh). Low-resolution mass spectra (MS) were measured on a Shimadzu GC-

MS-QP2010 mass spectrometer. High-resolution mass spectra (HRMS) were recorded in positive ion mode (ESI) using a Bruker micrOQTOF spectrometer. NMR spectra were recorded with Bruker DPX (^{1}H NMR = 400 MHz; ^{13}C NMR = 100 MHz) instruments using $CDCl_3$ as solvent and calibrated using tetramethylsilane (TMS) as internal standard. Coupling constants (*J*) were reported in Hertz and chemical shift (δ) in ppm. Optical rotations were measured with a JASCO P-2000 Polarimeter in CH_2Cl_2 solutions with percent concentrations.

General procedure for the synthesis of the selenol esters (**3a**-**h)**. In a single-neck round-bottom flask equipped with a rubber septum and with magnetic stirring containing a solution of the diselenide **1**[44] (0.194 g, 0.5 mmol), the apropriate anhydride **2a**-**h** (1.1 mmol) in PEG-400 (3.0 mL), Rongalite® (0.177 g, 1.5 mmol) and K_2CO_3 (0.069 g, 0.5 mmol) were added. The resulting mixture was stirred at room temperature and the reaction progress was followed by TLC. When the reaction was complete (the reaction time is indicated in Table 2), the mixture was added to water (50.0 mL) and extracted with ethyl acetate (3 x 15.0 mL). The combined organic layers were dried with $MgSO_4$, filtered and concentrated under vacuum. The crude product was purified by column chromatography on silica gel eluting with hexanes yielding the products **3a**-**h**. All the compounds are not described in the literature and were properly characterized by MS, ^{1}H NMR, ^{13}C NMR and HRMS.

General Procedure for the synthesis of water-soluble selenol ester 4a using Dowex-(H^+) resin.[50] To a solution of **3a** (0.299 g, 1.0 mmol) in MeOH (2.3 mL) was added Dowex® acidic ion-exchange resin (50WX8 20-50 mesh, 1.122 g). The reaction mixture was stirred for 24 h at room temperature and then the resin was filtered off and washed with MeOH. The filtrate was concentrated under vacuum and the crude was purified by column chromatography (50% EtOAc/hexanes) to afford the product **4a** as yellowish oil.

Water solubility. A weighted amount (0.090 g) of the compound **4a** was stirred in a vial at 25 ^{o}C, and water was added by syringe in 0.25 mL portions until complete solubilization.

***Se*-[(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]benzoselenoate (3a).** Yield: 0.210 g (70%); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$); δ (ppm): 7.91-7.89 (m, 2H); 7.60-7.56 (m, 1H); 7.46-7.42 (m, 2H); 4.38 (quint, *J* 6.1 Hz, 1H); 4.11 (dd, *J* 8.3 and 6.1 Hz, 1H); 3.69 (dd, *J* 8.3 and 6.1 Hz, 1H); 3.29 (d, *J* 6.1 Hz, 2H); 1.46 (s, 3H); 1.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$); δ (ppm): 193.7, 138.6, 133.7, 128.7, 127.1, 109.5, 75.0, 69.0, 28.1, 26.8, 25.5. MS *m*/*z* (rel. int., %) 285 (M^+, -CH_3, 0.5), 241 (3.9), 120 (7.5), 105 (100), 101 (2.0), 77 (47.4), 43 (35.7). HRMS: calculated mass to $C_{13}H_{16}O_3Se$: $[M + Na]^+$ 323.0157, found: 323.0168.

(*S*)-*Se*-[(2,2-Dimethy-1,3-dioxolan-4-yl)methyl]benzoselenoate ((*S*)-3a). Yield: 0.225 g (75%); yellow oil; $[\alpha]D^{20}$ +34.91 (*c* 0.53, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$); δ (ppm): 7.92-7.89 (m, 2H); 7.61-7.57 (m, 1H); 7.47-7.43 (m, 2H); 4.38 (quint, *J* 6.2 Hz, 1H); 4.12 (dd, *J* 8.4 and 6.2 Hz, 1H); 3.70 (dd, *J* 8.4 and 6.2 Hz, 1H); 3.30 (d, *J* 6.2 Hz, 2H); 1.46 (s, 3H); 1.36 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$); δ (ppm): 193.8, 138.6, 133.7, 128.8, 127.2, 109.6, 75.1, 69.1, 28.1, 26.9, 25.5. MS *m*/*z* (rel. int., %) 285 (M^+, -CH_3, 1.3), 241 (4.1), 120 (9.8), 105 (100), 101 (2.1), 77 (32.7), 43 (15.2). HRMS: calculated mass to $C_{13}H_{16}O_3Se$: $[M + Na]^+$ 323.0157, found: 323.0132

(*R*)-*Se*-[(2,2-Dimethy-1,3-dioxolan-4-yl)methyl]benzoselenoate ((*R*)-3a). Yield: 0.198 g (66%); yellow oil; $[\alpha]D^{20}$ -34.20 (*c* 0.51, CH_2Cl_2). The characterization data from NMR, MS and HRMS spectra were identical in all aspects with those of (*S*)-(+)-**3a** enantiomer.

***Se*-[(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]4-methylbenzoselenoate (3b).** Yield: 0.254 g (81%); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$); δ (ppm): 7.79 (d, *J* 8.8 Hz, 2H); 7.23 (d, *J* 8.8, 2H); 4.37 (quint, *J* 6.1 Hz, 1H); 4.10 (dd, *J* 8.4 and 6.1 Hz, 1H); 3.69 (dd, *J* 8.4 and 6.1 Hz, 1H); 3.28 (dd, *J* 6.1 and 6.1 Hz, 1H); 3.27 (dd, *J* 6.1 and 6.1 Hz, 1H); 2.38 (s, 3H); 1.46 (s, 3H); 1.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$); δ (ppm): 192.9, 144.6, 136.0, 129.3, 127.2, 109.4, 75.0, 69.0, 27.8, 26.8, 25.4, 21.5. MS *m*/*z* (rel. int., %) 299 (M^+, -CH_3, 0.6), 256 (5.6), 119 (100), 101 (1.4), 91 (31.3), 43 (13.9). HRMS: calculated mass to $C_{14}H_{18}O_3Se$: $[M + Na]^+$ 337.0313, found: 337.0312.

***Se*-[(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]4-bromobenzoselenoate (3c).** Yield: 0.268 g (71%); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$); δ (ppm): 7.77 (d, *J* 8.6 Hz, 2H); 7.60 (d, *J* 8.6 Hz, 2H); 4.38 (quint, *J* 6.2 Hz, 1H); 4.12 (dd, *J* 8.4 and 6.2 Hz, 1H); 3.69 (dd, *J* 8.4 and 6.2 Hz, 1H); 3.31 (dd, *J* 6.2 and 6.2 Hz, 1H); 3.29 (dd, *J* 6.2 and 6.2 Hz, 1H); 1.46 (s, 3H); 1.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$); δ (ppm): 192.9, 137.4, 132.1, 128.9, 128.6, 109.7, 74.9, 69.1, 28.5, 26.9, 25.50. MS *m*/*z* (rel. int., %) 362 (M^+, -CH_3, 1.1), 320 (7.0), 207 (3.3), 183 (100), 155 (27.3), 101 (6.0), 76 (28.1), 59 (10.6), 43 (53.9). HRMS: calculated mass to $C_{13}H_{15}BrO_3Se$: $[M + Na]^+$ 400.9262, found 400.9227.

***Se*-[(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]4-chlorobenzoselenoate (3d).** Yield: 0.184 g (55%); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$); δ (ppm): 7.83 (d, *J* 7.6 Hz, 2H); 7.42 (d, *J* 7.6 Hz, 2H); 4.37 (quint, *J* 6.1 Hz, 1H); 4.11 (dd, *J* 8.4 and 6.1 Hz, 1H); 3.68 (dd, *J* 8.4 and 6.1 Hz, 1H); 3.30 (d, *J* 6.1 Hz, 2H); 1.46 (s, 3H); 1.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$); δ (ppm): 192.5, 140.1, 136.9, 129.0, 128.4, 109.6, 74.9, 69.0, 28.4, 26.8, 25.4. MS *m*/*z* (rel. int., %) 319 (M^+, -CH_3, 1.4), 276 (7.9), 141 (33.2), 139 (100), 111 (32.5), 101 (4.0) 75 (18.4), 43 (43.5). HRMS: calculated mass to $C_{13}H_{15}ClO_3Se$: $[M + Na]^+$ 356.9767, found: 356.9765.

***Se*-[(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]2-chlorobenzoselenoate (3e).** Yield: 0.284 g (85%); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$); δ (ppm): 7.70-7.69 (m, 1H); 7.44-7.42 (m, 2H); 7.36-7.32 (m, 1H); 4.41 (quint, *J* 6.2 Hz, 1H); 4.14 (dd, *J* 8.4 and 6.2 Hz, 1H); 3.71 (dd, *J* 8.4 and 6.2 Hz, 1H); 3.32 (dd, *J* 6.2 and 6.2 Hz, 1H); 3.30 (dd, *J* 6.2 and 6.2 Hz, 1H); 1.46 (s, 3H); 1.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$); δ (ppm): 193.6, 138.6, 132.5, 131.0, 129.8, 129.0, 126.7, 109.6, 74.8, 69.0, 29.5, 26.8, 25.5. MS: *m*/*z* (rel. int.) 319 (M^+, -CH_3, 2.7), 276 (15.8), 141 (35.2), 139 (100), 111 (21.1), 101 (2.5), 75 (11.3), 43 (26.0). HRMS: calculated mass to $C_{13}H_{15}ClO_3Se$: $[M + Na]^+$ 356.9767, found: 356.9765.

***Se*-[(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]furan-2-carboselenoate (3f).** Yield: 0.203 g (70%); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$); δ (ppm): 7.62 (dd, *J* 1.7 and 0.8 Hz, 1H); 7.98 (dd, *J* 3.6 and 0.8 Hz, 1H); 6.56 (dd, *J* 3.6 and 1.7 Hz, 1H); 4.37 (quint, *J* 6.2 Hz, 1H); 4.10 (dd, *J* 8.4 and 6.2 Hz, 1H); 3.68 (dd, *J* 8.4 and 6.2 Hz, 1H); 3.27 (dd, *J* 6.2 and 6.2 Hz, 1H); 3.26 (dd, *J* 6.2 and 6.2 Hz, 1H); 1.45 (s, 3H); 1.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$); δ (ppm): 181.1, 152.0, 146.5, 114.9, 112.6, 109.6, 75.0, 69.0, 27.0, 26.8, 25.5; MS *m*/*z* (rel. int., %) 275 (M^+, -CH_3, 3.4), 120 (12.0), 95 (100), 67 (5.5), 43 (39.9). HRMS: calculated mass to $C_{11}H_{14}O_4Se$: $[M + Na]^+$ 312.9950, found: 312,9954.

***Se*-[(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]ethaneselenoate (3g).** Yield: 0.167 g (70%); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$); δ (ppm): 4.29 (quint, *J* 6.1 Hz, 1H); 4.07 (dd, *J* 8.4 and 6.1 Hz, 1H); 3.61 (dd, *J* 8.4 and 6.1 Hz, 1H); 3.10 (d, *J* 6.1 Hz, 2H); 2.43 (s, 3H); 1.43 (s, 3H), 1.34 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$); δ (ppm): 196.92, 109.52, 74.91, 68.98, 34.47, 28.41, 26.78, 25.43. MS *m*/*z* (rel. int., %) 223 (M^+, -CH_3, 2.6), 180 (8.5), 121 (14.4), 117 (5.1), 59 (11.2), 43 (100). HRMS: calculated mass to $C_8H_{14}O_3Se$: $[M + Na]^+$ 261.0000, found: 261.0007.

***Se*-[(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]2,2-dimethylpropaneselenoate (3h).** Yield: 0.202 g (72%); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$); δ (ppm): 4.25 (quint, *J* 6.2 Hz, 1H); 4.06 (dd, *J* 8.3 and 6.2 Hz, 1H); 3.60 (dd, *J* 8.3 and 6.2 Hz, 1H); 3.06 (dd, *J* 6.2 and 6.2 Hz, 1H); 3.04 (dd, *J* 6.2 and 6.2 Hz, 1H); 1.43 (s, 3H); 1.34 (s, 3H), 1.23 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$); δ (ppm): 208.8, 109.4, 75.2, 69.1, 49.3, 27.2, 26.9, 26.8, 25.5. MS: *m*/*z* (rel. int., %) 265 (M^+, -CH_3, 3.2), 222 (17.4), 136 (3.4), 116 (1.3), 107 (1.4), 72 (4.8), 57 (100), 43 (20.2). HRMS: calculated mass to $C_{11}H_{20}O_3Se$ $[M + Na]^+$ 303.0470, found: 303.0471.

***Se*-(2,3-Dihydroxypropyl) benzoselenoate (4a).** Yield: 0.205 g (79%); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$); δ (ppm): 8.35-8.33 (m, 2H); 8.05 -8.01 (m, 1H); 7.09-7.86 (m, 2H); 4.44-4.38 (m, 1H); 4.19 (dd, *J* 11.5 and 3.7 Hz, 1H); 4.08 (dd, *J* 11.5 and 6.0 Hz, 1H); 3.74 (dd, *J* 13.0 and 6.0 Hz, 1H); 3.66 (dd, *J* 13.0 and 6.5 Hz, 1H); 3.54 (brs, 2H). ^{13}C NMR (100 MHz, $CDCl_3$); δ (ppm): 195.48, 138.65, 133.84, 128.79, 127.25, 71.56, 65.51, 28.46; MS: *m*/*z* (rel. int., %) 241 (M^+, -OH, 0.2),138 (4.9), 105 (100), 77 (66.6). HRMS: calculated mass to $C_{10}H_{12}O_3Se$ $[M + Na]^+$ 282.9844, found: 282.9845.

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