(Z,Z)-Selanediylbis(2-propenamides): Novel Class of Organoselenium Compounds with High Glutathione Peroxidase-Like Activity. Regio- and Stereoselective Reaction of Sodium Selenide with 3-Trimethylsilyl-2-propynamides

Mikhail V. Andreev, Vladimir A. Potapov *, Maxim V. Musalov and Svetlana V. Amosova
A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Division of The Russian Academy of Sciences, 1 Favorsky Str., 664033 Irkutsk, Russia; miand@irioch.irk.ru (M.V.A.); musalov_maxim@irioch.irk.ru (M.V.M.); amosova@irioch.irk.ru (S.V.A.)
* Correspondence: v.a.potapov@mail.ru

Abstract: The efficient regio- and stereoselective synthesis of (Z,Z)-3,3′-selanediylbis(2-propenamides) in 76–93% yields was developed based on the reaction of sodium selenide with 3-trimethylsilyl-2-propynamides. (Z,Z)-3,3′-Selanediylbis(2-propenamides) are a novel class of organoselenium compounds. To date, not a single representative of 3,3′-selanediylbis(2-propenamides) has been described in the literature. Studying glutathione peroxidase-like properties by a model reaction showed that the activity of the obtained products significantly varies depending on the organic moieties in the amide group. Divinyl selenide, which contains two lipophilic cyclohexyl substituents in the amide group, exhibits very high glutathione peroxidase-like activity and this compound is considerably superior to other products in this respect.

Keywords: (Z,Z)-3,3′-selanediylbis(2-propenamides); 3-trimethylsilyl-2-propynamides; sodium selenide; glutathione peroxidase-like activity; regioselective reactions; stereoselective reactions; desilylation

1. Introduction

Vinyl selenides are important intermediates for organic synthesis [1–9]. These compounds have been used for the preparation of a number of valuable products [4–9]. Vinyl selenides have found application in the synthesis of functionalized ketones, (Z)-allyl alcohols, and unsaturated aldehydes [4]. The cross-coupling of vinyl selenides with terminal alkynes in the presence of a nickel/CuI catalyst at room temperature proceeded with of retention of stereochemical configuration leading to (Z)- and (E)-enyne derivatives in good yields [5]. The coupling reaction of vinyl selenides with Grignard reagents provided corresponding functionalized alkenes [6,7]. The synthesis of resveratrol and its methoxylated analogues—well known compounds due to their anti-inflammatory, anticancer, antibacterial, and neuroprotective activity, has been proposed based on vinyl selenides [8]. An efficient method for preparation of α-phenylselanyl lactones has been developed from α-(phenylseleno)vinyl tozylates [9].

Some vinyl selenides exhibit antioxidant [10], antinociceptive [11], and hepatoprotective activity [12].
The main methods for the preparation of vinyl selenides include a transition metal catalyzed coupling of vinyl halides with diselenides or selenols [13–16], reactions of thiols or chalcogenolates with selenoalkynes [14,17,18], and addition of selenium-centered nucleophiles to acetylenes [8,14,19–23].

One of the most useful and atom-economic methods is based on addition reactions of selenoles or selenolate anions with acetylenes [8,14,19–22]. Examples of these reactions refer mainly to vinyl selenides containing aliphatic or aromatic substituents at the β-carbon atom of the double bond. Examples of the synthesis of vinyl selenides bearing electron-withdrawing groups are scarce in the literature. The synthesis of (Z,Z)-bis(2-acyvlnyl) selenides by the addition reaction of sodium selenide with organyl ethynyl ketones was developed [23].

There are only a few representatives of vinyl selenides containing the amide group [24–27]. The Pd-catalyzed four-component reaction between sulfonamide, alkyne, diphenyl diselenide, and carbon monoxide afforded substituted 3-(phenylselenyl)propenamides in 65–90% yields [24]. Functionalized 3-(phenylselenyl)propenamides were obtained in 57–89% yields based on 3-(phenylselenyl)acrylic acid which was synthesized in 65% yield from diphenyl diselenide and ethyl propiolate [25]. The reaction of carbamoylsonoate, PhSeC(O)NMe2, with 1-octyne in the presence of Pd(PPh3)4 gave 3-hexyl-3-(phenylselenyl)propenamide in 40% yield [26].

There are no data in the literature about the biological activity of 3-selanylpropenamides. However, it is known that vinyl sulfides bearing the amide group in the β-position exhibit anticancer [28] and antifungal [29] activity (Figure 1). Containing the 2-amidovinylsulfonyl group methylgerambullone (isolated from Glycosmis angustifolia) acts as the agonist of acetylcholine receptors [30]. Phenoxyquinolines bearing a 2-amidovinylsulfonyl moiety shows the properties of c-Met kinase inhibitors [31] (Figure 1).

Taking into account the indicated biological properties of 3-sulfanlypropanamides, it can be assumed that selenium analogs of these compounds can also display some kinds of biological activity. Moreover, the vinylamide group, itself, is an important part of some biologically active natural compounds and pharmaceuticals, which exhibit antitumor, anti-tuberculosis, and anticonvulsant activity [32–36].

Figure 1. Known biologically active derivatives of vinyl sulfides containing the amide group (anticancer [28], antifungal [29], agonist of acetylcholine receptors [30], c-Met kinase inhibitor [31]).

To date, considerable effort has been devoted to the discovery of compounds that mimic the action of selenium-containing glutathione peroxidase enzymes [37–47]. The presence of selenium in these enzymes largely determines the glutathione peroxidase activity. In particular, organoselenium compounds bearing amide groups have been shown to be good catalysts for the reduction of peroxides and hydroperoxides with thiols (Figure 2).
Ebselen, which contains the selenenamide function in the cycle, and its analog ethaselen and propylselen show high glutathione peroxidase mimetic properties [37–41]. Additionally, ebselen exhibits anti-inflammatory and neuroprotective activity. These properties combined with glutathione peroxidase-like activity and relatively low toxicity of ebselen has led to therapeutic application of this compound, which has undergone evaluation in clinical trials as an anti-inflammatory agent [42]. This compound is also used for the treatment and prevention of cardiovascular diseases and ischemic stroke [41].

The range of bearing amide group organoselenium compounds, which exhibit glutathione peroxidase activity, comprises 1,2-benzoselenazin-3-ones (including the homologue of ebselen, 2-phenyl-1,2-benzoselenazin-3-one), 1,2-selenazolan-3-ones, benzoselenazolinones, and seleninic acid anhydride (which has been synthesized based on salicylic acid amide and selenium tetrachloride) [41–44] (Figure 2).

Camphor-derived selenenamide was synthesized by action of bromine on corresponding camphor diselenide, which was obtained based on the reaction of camphor enolate with selenium [42]. The glutathione peroxidase mimetic property of the camphor derived selenenamide was studied using a model reaction of benzenemethanethiol oxidation by tert-butyl hydroperoxide in the presence of the selenenamide as a catalyst (10% mol) in dichloromethane or deuterochloroform at room temperature. A similar model reaction of benzenemethanethiol oxidation by hydrogen peroxide was applied to examine the glutathione peroxidase-like activity of containing hydroxy group divinyl selenides as a catalysts (10% mol) [45]. The progress of the reaction was monitored by $^1$H NMR spectroscopy.

Previously we developed efficient syntheses of vinyl and divinyl selenides based on the addition of selenium-containing reagents, including sodium selenide, to the triple bond of acetylene and its derivatives [23,27,48–57].

To date, the reactions of sodium selenide with neither 2-propynamides nor 3-(triorganylsilyl)-2-propynamides have yet been described in the literature. It is known that the introduction of electron-donating triorganylsilyl group at the triple bond changes the reactivity of acetylene derivatives and deactivates the triple bond toward nucleophilic addition [58].

In order to develop the method for preparation of previously unknown divinyl selenides containing amide groups we studied the reaction of sodium selenide with 3-(trimethylsilyl)-2-propynamides and found the conditions for regio- and stereoselective addition. The obtained results are described in the present work.

2. Results and Discussion

Recently we realized the addition of sodium benzeneselenolate to 3-(trimethylsilyl)-2-propynamides containing morpholine and phenylamide moieties (Scheme 1) [27]. The reaction was...
carried out by addition of sodium borohydride to a stirred solution of 3-trimethylsilyl-2-propynamides and diphenyl diselenide in a THF–water (4/1) system at room temperature and accompanied by desilylation. The generation of sodium benzeneselenolate occurred in situ followed by nucleophilic addition of this highly reactive intermediate to the triple bond.

\[
\text{Ph}_2\text{Se}_2 \xrightarrow{\text{NaBH}_4/\text{THF/H}_2\text{O}} 2 \text{PhSeNa}
\]

\[
\text{NR}^1\text{R}^2 = \text{NHPh}, \text{N}(\text{C}_2\text{H}_4\text{)}_2\text{O}
\]

Scheme 1. Synthesis of containing the amide group vinyl selenides from diphenyl diselenide and 3-(trimethylsilyl)-2-propynamides.

The reaction proceeded in stereo- and regioselective manners affording (Z)-N-phenyl-3-(phenylselanyl)prop-2-enamide (72% yield) and (Z)-1-morpholino-3-(phenylselanyl)prop-2-en-1-one (70% yield), which were isolated as colorless crystalline compounds [27]. To the best of our knowledge, these are first examples of the addition of organylselenolates to 3-silyl-2-propynamides.

The commonly used conditions for generation of organylselenolates from corresponding diselenides and sodium selenide from elemental selenium consist in the application of sodium borohydride as a reducing agent and carrying out the reaction in alcohols [59]. However, when the reactions of sodium benzeneselenolate or sodium selenide with 3-(trimethylsilyl)-2-propynamides proceeded in methanol or ethanol, the formation of 3-alkoxy-2-propenamides as by-products was observed. The possibility of the formation of 3-alkoxy-2-propenamides from 3-(trimethylsilyl)-2-propynamides in reactions with alcohols has been previously described [60].

We found that the THF–water system is preferable in addition reactions of selenium-centered nucleophiles with 3-(trimethylsilyl)-2-propynamides compared to commonly used alcohol conditions. The yields of the target products are higher and 3-alkoxy-2-propenamides are not formed as by-products.

The addition reactions of selenide anion with propynamides and 3-silyl-2-propynamides have not yet been described in the literature. In order to obtain previously unknown divinyl selenides containing amide groups we studied the addition of sodium selenide to 3-(trimethylsilyl)-2-propynamides bearing various groups (phenyl, alkyl, cyclohexyl, morpholine and piperidine) in the amide moieties (Scheme 2). Sodium selenide was efficiently generated from elemental selenium and sodium borohydride in water and used without isolation in further nucleophilic addition reactions.

The conditions for the regio- and stereoselective reaction of 3-trimethylsilyl-2-propynamides 1a–i with sodium selenide were found. The reaction proceeded in the THF–water system under argon affording (Z,Z)-3,3′-selanediylbis(2-propynamides) 2a–i in 76-93% yields (Scheme 2).
Which are soluble in THF. The ratio of the solvents in the THF–water system was varied from 1/3 to 3/1 (methods A and B). In the method A, a solution of silylpropynamides in THF was added to a hot aqueous solution of sodium selenide and the mixture was refluxed for 10 min. In the case of method B, sodium borohydride was added portionwise to a mixture of propynamides and selenium, and the mixture was refluxed for 10 min. Yields: 25–93%. Method C: Sodium borohydride was added portionwise to a mixture of 3-(trimethylsilyl)-2-propynamide, selenium, and water (Methods A and B). Sodium selenide was obtained by addition of an aqueous solution of sodium selenide to a hot mixture of selenium and water (Methods A and B). Yields: 76–91%.

Water is necessary for generating sodium selenide and reacting Na2Se with propynamides 1a–i which are soluble in THF. The ratio of the solvents in the THF–water system was varied from 1/3 (method A) to 3/1 (method B). In the method A and B, a solution of silylpropynamides in THF was added to a hot aqueous solution of sodium selenide, which was obtained from elemental selenium and sodium borohydride, and the mixture was refluxed for 10 min. In the case of method C, sodium borohydride was added portionwise to a mixture of propynamides 1b–d,f–i and selenium in the THF–water system (the ratio of the solvents 4/1) and the mixture was stirred at room temperature for 4 h (10 h for 2g).
Best yields of the products were obtained when the reaction mixtures were refluxed for 10 min in the THF–water system. When reaction was carried out at room temperature, the yields dropped despite increasing the reaction duration. The divinyl selenides 2b–d, f–i were obtained in 50–73% yields with 4 h stirring at room temperature under argon (Scheme 2, method C). Surprisingly, neither unconverted 3-(trimethylsilyl)-2-propynamides 1b–d, f–i nor desilylated propynamides were detected in the reaction mixture in these cases after completion of the reaction (method C). However, the yields of the target products 2b–d, f–i were lower than in the methods A and B.

The reaction of sodium selenide with propynamide 1f bearing two phenyl substituents in the amide group under the conditions of method A led to a mixture containing divinyl selenide 2f in 25% yield, unconverted silylpropynamide 1f (31% conversion) and the desilylated amide, N,N-diphenyl-2-propynamide (1%). The reaction of sodium selenide with silylpropynamide 1g containing two cyclohexyl moieties in the amide group also gave similar poor results. We supposed that the reason of the insufficient yield of selenides 2f,g and low conversion of starting amides 1f,g may be poor solubility of propynamides 1f,g in the mixture water–THF (3/1, method A) due to lipophilic organic moieties of the amide group. The silylpropynamides 1f,g are insoluble in water but soluble in THF. Indeed, when the method B (THF–water 3/1) was applied, products 2f,g were obtained in 76–77% yields. The method A was found to provide high yields of products 2c–e,h,i (85–93%) derived from silylpropynamides 1c–e,h,i containing monophenyl, dialkyl, morpholine, and piperidine moieties in the amide group.

The possible pathway for the formation of products 2a–i can include both the addition—desilylation processes and the sequential desilylation—addition reactions via the generation of intermediate propynamides 3a–i (Scheme 3). The addition of sodium selenide to the triple bond of silylpropynamides 1a–i is accompanied by the formation of sodium hydroxide, which acts as the catalyst for the desilylation reaction. We suppose that the desilylation process can proceed on different stages of the reaction including various intermediate species (Scheme 3).

![Scheme 3](image)

Scheme 3. The possible reaction pathways for the formation of products 2a–i.

The formation of intermediate 2-propynamides 3a–i in very small amounts (before the isolation of the reaction products 2a–i) was registered in the reaction mixture by NMR. The NMR data of the intermediate propynamides 3a–i coincide with the spectral characteristics of the previously obtained samples of these compounds, which were synthesized by desilylation of silylpropynamides 1a–i [60].

The formation of propynamides 3a–i in the reaction (Scheme 2) indicates the possibility of the reaction pathway via desilylation of silylpropynamides 1a–i. It was previously established that silylpropynamides 1a–i can be desilylated by the action of various reagents (potassium fluoride, alkali metal hydroxides and other bases) and converted to corresponding propynamides 3a–i [60].

It is worth noting that the application of 3-trimethylsilyl-2-propynamides 1a–i as the initial substrates in the preparation of the target vinyl selenides is preferable compared to 2-propynamides with the terminal triple bond. The latter compounds are hardly available and the price for these chemicals is very high. Their preparation is usually based on toxic and skin-irritating propynoic
acid. The silylpropynamides 1a–i were synthesized in the present work by the method depicted in Scheme 4 [61–63]. Inexpensive starting propargyl alcohol, good selectivity of these reactions and high yield of the target products allowed to make silylpropynamides 1a–i readily available compounds and to use them in the synthesis of valuable products [64–66].

![Scheme 4](image)

Scheme 4. The method for the preparation of 3-trimethylsilyl-2-propynamides 1a–i.

The obtained selanediylbis(2-propynamides) 2a–i are a novel class of organoselenium compounds. Like ebselen and some organoselenium compounds, which exhibit glutathione peroxidase-like activity (Figure 2), products 2a–i contain the amide function, and their activity deserved to be studied.

We studied glutathione peroxidase-like activity of the obtained products 2a–i using the model reaction of benzenemethanethiol oxidation [42,45] by tert-butyl hydroperoxide (TBHP) in the presence of compounds 2a–i as catalysts and the progress of this reaction was monitored by 1H NMR spectroscopy. First experiments in the NMR tubes (TBHP, BnSH, 0.1 mmol, deuterochloroform) at room temperature showed that the reactions proceeded too fast when 10% mol of the catalysts were used. In order to realize the 1H NMR monitoring, the amounts of the catalysts were decreased to 0.5% mol. Diphenyl diselenide was used as the standard compound (this compound is often used as the standard catalyst for in these experiments [42–47]).

It was found that the activity of the obtained products 2a–i varies significantly depending on the organic moieties in the amide group. The results of studying the compounds 2d,f,g,h,i, which outperform diphenyl diselenide in the glutathione peroxidase-like activity, are presented in Figure 3 (a 24 h scale) and Figure 4 (a 90 min scale). In the control experiment, under the same reaction conditions but in the absence of the catalyst, the conversion of phenylmethanethiol was only about 4% after 24 h according to 1H NMR data.

Product 2g containing two lipophilic cyclohexyl substituents in the amide group shows highest glutathione peroxidase-like properties (Figures 4 and 5). This compound is significantly superior to other products in activity. The second most active product is compound 2i (Figure 4) bearing the piperidine moieties in the amide function and the third is product 2d (the activity of which is presented in both Figures 3 and 4). Compounds 2f,h containing the morpholine and phenyl moieties also exhibit higher activity compared to diphenyl diselenide.

The obtained results are very promising. However, the interpretation of the influence of organic moieties on the catalytic activity and discussion on possible intermediates of the catalytic cycle requires additional data and further research.
Figure 3. Studying glutathione peroxidase-like activity of compounds 2d, f, h by $^1$H NMR monitoring with the use of Ph$_2$Se$_2$ as the standard compound (TBHP, BnSH, 0.1 mmol, deuterochloroform, 0.5% mol of studied compounds). The control experiment was carried out in the absence of studied compounds.

Figure 4. Studying glutathione peroxidase-like activity of compounds 2d, g, i (TBHP, BnSH, 0.1 mmol, deuterochloroform, 0.5% mol of studied compounds) by $^1$H NMR monitoring.

Figure 5. Compounds 2d, f, g, h, i exhibiting higher glutathione peroxidase-like activity compared to Ph$_2$Se$_2$ (the compounds are arranged in the decreasing order of the activity).
3. Experimental Section

3.1. General Information

The $^1$H (400.1 MHz), $^{13}$C (100.6 MHz) and $^{77}$Se (76.3 MHz) NMR spectra (Supplementary Materials) were recorded on a Bruker DPX-400 spectrometer (Bruker BioSpin GmbH, Rheinstetten, Germany) in CDCl$_3$ and $d_6$-DMSO 5–10% solutions and referred to TMS ($^1$H, $^{13}$C) and dimethyl selenide ($^{77}$Se). The IR spectra were taken on a Bruker IFS-25 spectrometer (Bruker BioSpin GmbH, Rheinstetten, Germany). Mass spectra were recorded on a Shimadzu GCMS-QP5050A (Shimadzu Corporation, Kyoto, Japan) with electron impact (EI) ionization (70 eV). Elemental analysis was performed on a Thermo Scientific Flash 2000 Elemental Analyzer (Thermo Fisher Scientific Inc., Milan, Italy). Melting points were determined on a Kofler Hot-Stage Microscope PolyTherm A apparatus (Wagner & Munz GmbH, München, Germany). The organic solvents were dried and distilled according to standard procedures. Silica gel (Alfa Aesar, 0.06–0.20 mm (70–230 mesh)) and ethyl acetate–methanol (10:1) as an eluent were used for column chromatography.

3.2. Method A (Preparation of Compounds 2c–f,h,i)

A mixture of elemental selenium (19 mg, 0.24 mmol) and degassed water (4.0 mL) was heated on a water bath (90–95 °C) and a solution of NaBH$_4$ (40 mg, 1.05 mmol) in degassed water (0.5 mL) was added under argon. After dissolution of selenium and the formation of colorless mixture, a solution of 3-trimethylsilyl-2-propynamide (0.48 mmol) in THF (1.5 mL) was added to a hot aqueous solution of the sodium selenide and the mixture was refluxed for 10 min (5 h for 1g) under argon. The mixture was cooled by cold water bath and extracted with CH$_2$Cl$_2$ ($3 \times 7.0$ mL). The organic phase was dried over Na$_2$SO$_4$ and the solvent was removed under reduced pressure. General yields: 85–93%.

3.3. Method B (Preparation of Compounds 2a,b,f,g)

A mixture of elemental selenium (19 mg, 0.24 mmol) and degassed water (2.0 mL) was heated on a water bath (90–95 °C) and a solution of NaBH$_4$ (40 mg, 1.05 mmol) in degassed water (0.4 mL) was added under argon. After dissolution of selenium and the formation of colorless mixture, a solution of 3-trimethylsilyl-2-propynamide (0.48 mmol) in THF (1.5 mL) was added to a hot aqueous solution of the sodium selenide and the mixture was refluxed for 10 min (5 h for 1g) under argon. The mixture was cooled by cold water bath and THF was removed by a rotary evaporator. The residue was extracted with CH$_2$Cl$_2$ (3 × 7.0 mL). The organic phase was dried over Na$_2$SO$_4$ and the solvent was removed under reduced pressure. General yields: 76–91%.

3.4. Method C (Preparation of Compounds 2a–i)

NaBH$_4$ (30 mg, 0.79 mmol) was added portionwise to a stirred mixture of selenium (19 mg, 0.24 mmol), 3-trimethylsilyl-2-propynamide (0.48 mmol), degassed water (0.5 mL) and THF (2.0 mL). The mixture was stirred at room temperature for 5 h under argon and degassed water (2 mL) was added. The mixture was extracted with CH$_2$Cl$_2$ (3 × 7.0 mL). The organic phase was dried over Na$_2$SO$_4$ and the solvent was removed under reduced pressure. General yields: 50–74%.

3.5. Compounds 2a–i

(Z)-3-[(Z)-3-amino-3-oxo-1-propenyl]selanyl-2-propenamide (2a) was prepared by the method B (91% yield) and the method C (72% yield). After refluxing for 10 min, the solvent was removed under reduced pressure and product 2a was extracted from the residue by boiling acetone. The solvent was removed under reduced pressure giving 2a (48 mg, 91%, method B); (38 mg, 72%, method C); yellowish powder; mp 183–184 °C. $^1$H NMR (400 MHz, $d_6$-DMSO): $\delta$ 6.38 (d, $^3$J = 9.5 Hz, 2H, =CHCO), 7.10 (s, 2H, NH$_2$), 7.50 (s, 2H, NH$_2$), 7.65 (d, $^3$J = 9.5 Hz, 2H, Se=CH=). $^{13}$C NMR (100 MHz, $d_6$-DMSO): $\delta$ 120.6 (Se=CO), 145.3 (Se=C), 128.2 Hz), 168.1 (C=O). $^{77}$Se NMR (76 MHz, $d_6$-DMSO): $\delta$ 507.4. IR (KBr): 3430,
(Z)-N-methyl-3-[(Z)-3-(dimethylamino)-3-oxo-1-propenyl]selanyl-2-propenamide (2b) was prepared by the method B (80% yield) and the method C (71% yield). After addition of degassed water to the reaction mixture, the precipitate was filtered and dried in vacuum giving product 2b (47.5 mg, 80%, method B); (42 mg, 71%, method C); white powder; mp 215–216 °C. 1H NMR (400 MHz, d6-DMSO): δ 2.64 (d, 3J) = 4.4 Hz, 6H, CH3), 6.35 (d, 3J = 9.6 Hz, 2H, =CHCO), 7.59 (d, 3J = 9.6 Hz, 2H, SeCH=), 8.01 (q, 3J = 4.4 Hz, 2H, NH). 13C NMR (100 MHz, d6-DMSO): δ 25.5 (CH3), 120.4 (=CCO), 144.0 (SeC=, 1Se-C = 127.4 Hz), 166.8 (C=O). 77Se NMR (76 MHz, d6-DMSO): δ 502.7. IR (KBr): 3324, 3041, 2938, 1644 (C=O), 1580 (C=C), 1413, 1244, 1148, 1057, 805, 725, 698, 653 cm⁻¹. MS (EI), m/z (%): 248 (20) [M]+, 246 (9), 187 (6), 166 (9), 164 (43), 162 (30), 161 (25), 147 (92), 145 (45), 143 (22), 135 (9), 134 (15), 133 (10), 132 (7), 131 (7), 110 (11), 107 (13), 106 (15), 105 (8), 104 (9), 84 (100), 68 (17), 66 (7), 58 (96), 51 (15), 55 (15), 53 (13), 44 (14), 43 (9), 42 (19), 41 (10). Anal. calcd for C18H16N2O2Se (247.15): C 38.88, H 4.89, N 11.33, Se 31.95%. Found: C 38.91, H 4.86, N 11.57, Se 32.14%.

(Z)-N-phenyl-3-[(Z)-3-(diethylamino)-3-oxo-1-propenyl]selanyl-2-propenamide (2c) was prepared by the method A (85% yield) and the method C (69% yield). After removing the solvent, the residue was dissolved in THF with cold hexane giving product 2c which was dried in vacuum (76 mg, 85%, method A); (61 mg, 69%, method C); beige powder; mp 219–220 °C. 1H NMR (400 MHz, d6-DMSO): δ 6.65 (d, 3J = 9.6 Hz, 2H, =CHCO), 7.06 (t, 3J = 7.7 Hz, 2H, H6)', 7.32 (dd, 3J = 7.7 Hz, 4H, H5, H4), 7.66 (d, 3J = 7.7 Hz, 4H, H3), 7.94 (d, 3J = 9.6 Hz, 2H, SeCH=), 10.23 (s, 2H, NH). 13C NMR (100 MHz, d6-DMSO): δ 119.0 (=CCO), 121.0 (C=C), 123.4 (C=C), 128.9 (C=), 139.1 (C=C), 146.7 (SeC=, 1Se-C = 129.0 Hz), 164.9 (C=O). 77Se NMR (76 MHz, d6-DMSO): δ 518.8. IR (KBr): 3266, 3129, 3039, 2929, 1636 (C=O), 1603 (C=C, Ph), 1544 (C=C, Ph), 1499 (C=C=C, Ph), 1439, 1365, 1302, 1247, 1201, 1159, 979, 794, 648, 594, 505 cm⁻¹. MS (EI), m/z (%): 372 (8) [M]+, 224 (15), 211 (9), 209 (47), 207 (23), 206 (9), 205 (9), 187 (6), 161 (18), 159 (11), 147 (13), 146 (100), 145 (12), 138 (3), 132 (31), 131 (6), 129 (8), 120 (8), 117 (14), 106 (8), 104 (12), 94 (11), 93 (79), 92 (29), 91 (9), 77 (37), 66 (11), 65 (34), 64 (7), 51 (11), 39 (17). Anal. calcd for C18H16N2O2Se (371.29): C 58.23, H 4.34, N 7.54, Se 21.27%. Found: C 58.50, H 4.29, N 7.48, 20.97%.

(Z)-3-[(Z)-3-(dimethylamino)-3-oxo-1-propenyl]selanyl-N,N-dimethyl-2-propenamide (2d) was prepared by the method A (86% yield) and the method C (68% yield). After removing the solvent, the residue was dissolved in CHCl3 and precipitated with cold hexane giving product 2d, which was dried in vacuum (57 mg, 86%, method A); (46 mg, 68%, method C); white powder; mp 181–182 °C. 1H NMR (400 MHz, CDCl3): δ 3.01, 3.06 (s, 12H, CH3), 6.74 (d, 3J = 9.7 Hz, 2H, =CHCO), 7.52 (d, 3J = 9.7 Hz, 2H, SeCH=). 13C NMR (100 MHz, CDCl3): δ 35.4, 37.2 (CH3), 116.8 (=CCO), 147.6 (SeC=, 1Se-C = 132.6 Hz), 166.9 (C=O). 77Se NMR (76 MHz, CDCl3): δ 516.8. IR (KBr): 3024, 2925, 2861, 1624 (C=O), 1572 (C=C), 1492, 1403, 1324, 1261, 1146, 1065, 986, 781, 694, 591, 523 cm⁻¹. MS (EI), m/z (%): 276 (8) [M]+, 195 (10), 187 (8), 178 (25), 176 (12), 161 (7), 124 (8), 106 (6), 98 (71), 72 (100), 70 (9), 55 (9), 46 (12), 44 (29), 15 (42). Anal. calcd for C10H16N2O2Se (275.21): C 43.64, H 5.86, N 10.18, Se 28.69%. Found: C 43.71, H 5.63, N 10.29, Se 28.54%.

(Z)-3-[(Z)-3-(diethylamino)-3-oxo-1-propenyl]selanyl-N,N-diethyl-2-propenamide (2e) was prepared by the method A (86% yield) and the method C (72% yield). After removing the solvent, residue was dissolved in CHCl3 and precipitated with cold hexane in a refrigerator (–18 °C) giving product 2e which was dried in vacuum (68 mg, 86%, method A); (57 mg, 72%, method C); pale yellow solid; mp 56–57 °C. 1H NMR (400 MHz, CDCl3): δ 1.12 (t, 3J = 6.8 Hz, 12H, CH3), 3.32, 3.38 (q, 3J = 6.8 Hz, 8H, CH2), 6.64 (d, 3J = 9.7 Hz, 2H, =CHCO), 7.47 (d, 3J = 9.7 Hz, 2H, SeCH=). 13C NMR (100 MHz, CDCl3): δ 13.2, 14.8 (CH3), 40.6, 42.1 (CH2), 117.1 (=CCO), 147.5 (SeC=, 1Se-C = 131.9 Hz), 166 (C=O). 77Se NMR (76 MHz, CDCl3): δ 519.4. IR (KBr): 3027, 2975, 2930, 2901, 2873, 1618 (C=O), 1566 (C=C), 1481, 1448, 1428, 1376,
(Z)-3-[[Z]-3-(diphenylamino)-3-oxo-1-propenyl]selanyl-N,N-diphenyl-2-propenamide (2f) was prepared by the method A (25% yield), the method B (76% yield) and the method C (66% yield). After removing the residue, the residue was dissolved in CHCl₃ and precipitated with cold hexane giving product 2f which was dried in vacuum (31 mg, 25%, method A); (96 mg, 76%, method B); (83 mg, 66%, method C); beige powder; mp 201–203 °C. ¹H NMR (400 MHz, CDCl₃): δ 6.35 (d, 3J = 9.7 Hz, 2H, =CHCO), 7.23–7.30 (m, 12H, H²), 7.32–7.40 (m, 8H, H⁶), 7.48 (d, 3J = 9.7 Hz, 2H, SeCH=). ¹³C NMR (100 MHz, CDCl₃): δ 119.6 (=CCO), 125.1–128.6 (C⁴⁵), 129.2 (C²), 142.6 (C'), 149.2 (SeC=, 1JS=Se = 133.9 Hz), 166.3 (C=O). ⁷²Se NMR (76 MHz, CDCl₃): δ 533.3. IR (KBr): 2929, 1635 (C=O), 1552 (C= C, Ph), 1492, 1370, 1269, 1164, 1035, 782, 695, 543 cm⁻¹. MS (EI), m/z (%): 523 (2) [M]+, 303 (6), 222 (14), 209 (20), 208 (100), 196 (9), 180 (29), 170 (9), 169 (61), 168 (38), 167 (44), 166 (6), 77 (19). Anal. calc for C₃₀H₂₄N₂O₂Se (523.48): C 68.83, H 4.62, N 5.35, Se 15.08%. Found: C 68.65, H 4.47, N 5.56, Se 15.04%.

(Z)-3-[[Z]-3-(dicyclohexylamino)-3-oxo-1-propenyl]selanyl-N,N-dicyclohexyl-2-propenamide (2g) was prepared by the method B (refluxing for 5 h, 77% yield) and method C (stirring at room temperature for 10 h, 50% yield). After removing the solvent, the residue was recrystallized from benzene (101 mg, 77%, method A); (66 mg, 50%, method C); white powder; mp 127–129 °C. ¹H NMR (400 MHz, CDCl₃): δ 1.03–1.38, 1.44–1.90 (m, 36H, H), 2.12–2.27 (m, 4H, H), 3.37–3.54 (m, 4H, H), 6.70 (d, 3J = 9.7 Hz, 2H, =CHCO), 7.39 (d, 3J = 9.7 Hz, 2H, SeCH=). ¹³C NMR (100 MHz, CDCl₃): δ 24.4 (C₃³), 25.4 (C₃₅), 29.4, 30.6, 31.0 (C²₄), 54.5, 56.0 (C¹), 118.8 (=CCO), 145.0 (SeC=, 1JS=Se = 130.6 Hz), 165.4 (C=O). ⁷²Se NMR (76 MHz, CDCl₃): δ 508.7. IR (KBr): 2926, 2852, 2663, 1614 (C=O), 1559 (C= C, O), 1465, 1439, 1389, 1366, 1342, 1291, 1264, 1233, 1181, 1141, 1126, 1053, 996, 896, 779, 714, 637, 619, 595, 504. MS (EI), m/z (%): 549 (4) [M]+, 314 (20), 312 (10), 286 (6), 235 (19), 234 (89), 232 (9), 181 (8), 180 (44), 178 (6), 161 (10), 152 (47), 150 (19), 148 (7), 138 (19), 98 (69), 96 (11), 83 (49), 82 (9), 81 (18), 79 (8), 70 (12), 67 (9), 56 (21), 55 (100), 44 (10), 43 (8), 41 (42). Anal. calc for C₃₀H₄₈N₂O₂Se (547.67): C 65.79, H 8.83, N 5.11, Se 14.42%. Found: C 65.63, H 8.82, N 4.96, Se 14.38%.

(Z)-1-morpholino-3-[[Z]-3-morpholino-3-oxo-1-propenyl]selanyl-2-propen-1-one (2h) was prepared by the method A (93% yield) and the method C (73% yield). After removing the solvent, residue was dissolved in CHCl₃ and precipitated with cold hexane (80 mg, 93%, method A); (63 mg, 73%, method C); white powder; mp 196–197 °C. ¹H NMR (400 MHz, CDCl₃): δ 3.55 (br m, 4H, H²), 3.69 (br m, 12H, H²), 6.72 (d, 3J = 9.7 Hz, 2H, =CHCO), 7.59 (d, 3J = 9.7 Hz, 2H, SeCH=). ¹³C NMR (100 MHz, CDCl₃): δ 42.1, 46.0 (C₃³), 66.8 (C²), 116.0 (=CCO), 148.7 (SeC=, 1JS=Se = 132.2 Hz), 165.7 (C=O). ⁷²Se NMR (76 MHz, CDCl₃): δ 520.2. IR (KBr): 2957, 2910, 1616 (C=O), 1563 (C= C), 1437, 1235, 1113, 1035, 964, 786, 602, 572 cm⁻¹. Anal. calc for C₁₄H₂₄N₂O₂Se (359.28): C 46.80, H 5.61, N 7.80, Se 21.98%. Found: C 46.96, H 5.39, 7.95, Se 21.60%. MS (EI), m/z (%): 549 (4) [M]+, 279 (11), 220 (27), 218 (13), 187 (14), 166 (11), 159 (15), 161 (26), 159 (14), 141 (11), 140 (100), 135 (9), 134 (9), 133 (10), 132 (7), 131 (8), 124 (6), 114 (79), 107 (7), 106 (8), 88 (17), 87 (16), 86 (99), 82 (13), 70 (77), 57 (17), 56 (55), 55 (30), 54 (9), 53 (9), 45 (8), 44 (6), 43 (6), 42 (40), 41 (10).

(Z)-3-[[Z]-3-piperidino-3-oxo-1-propenyl]selanyl-1-piperidino-2-propen-1-one (2i) was prepared by the method A (89% yield) and the method C (65% yield). After removing the solvent, residue was dissolved in CHCl₃ and precipitated with cold hexane (77 mg, 89%, method A); (55 mg, 65%, method C); beige powder; mp 208–209 °C. ¹H NMR (400 MHz, CDCl₃): δ 1.53–1.61 (m, 8H, H²), 1.61–1.70 (m, 4H, H⁴), 3.49, 3.61 (br m, 8H, H²), 6.75 (d, 3J = 9.8 Hz, 2H, =CHCO), 7.49 (d, 3J = 9.8 Hz, 2H, SeCH=). ¹³C NMR (100 MHz, CDCl₃): δ 24.7 (C¹), 25.6, 26.7 (C₅₃), 42.9, 46.8 (C²), 117.0 (=CCO), 147.1 (SeC=, 1JS=Se = 131.0 Hz), 165.5 (C=O). ⁷²Se NMR (76 MHz, CDCl₃): δ 508.7. IR (KBr): ν 2931, 2853, 1608 (C=O), 1562 (C=C), 1442, 1374, 1243, 1225, 1128, 1012, 955, 788, 658, 631, 602, 538 cm⁻¹. MS (EI), m/z (%): 556 (4) [M]+, 218 (7), 161 (9), 138 (47), 112 (14), 84 (100), 69 (17), 56 (12), 55 (14), 42 (9), 41 (23).

Molecules 2020, 25, 5940
Anal. calcd for C₁₆H₂₄N₂O₂Se (355.33): C 54.08, H 6.81, N 7.88, Se 22.22%. Found: C 53.81, H 6.82, N 7.91, Se 22.03%.

4. Conclusions

The efficient regio- and stereoselective synthesis of a novel class of organoselenium compounds, (Z, Z)-3,3′-selanediylbis(2-propenamides), based on the reaction of sodium selenide with 3-trimethylsilyl-2-propynamides was developed. Not a single representative of 3,3′-selanediylbis(2-propenamides) has yet been described in the literature. Studying their glutathione peroxidase-like properties by a model reaction showed that compounds 2g, i, d exhibit high activity. It was found that the glutathione peroxidase-like activity of the obtained products varies significantly depending on the organic moieties in the amide group. Containing two lipophilic cyclohexyl substituents in the amide group compound 2g is significantly superior to other products in activity. The second most active product is compound 2i bearing the piperidine moieties in the amide function. Containing the morpholine and diphenyl moieties compounds 2f, h also exhibit higher catalytic activity compared to diphenyl diselenide.

Supplementary Materials: The following are available online, the NMR spectra of the obtained compounds.

Author Contributions: Research experiments: M.V.A.; methodology, conceptualization, and the paper preparation: V.A.P.; studying GPx-like activity: M.V.M.; data curation: S.V.A. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by Russian Science Foundation, grant number 18-13-00372.

Acknowledgments: The authors thank Baikal Analytical Center SB RAS for providing the instrumental equipment for structural investigations.

Conflicts of Interest: The authors declare no conflict of interest.

References
1. Perin, G.; Lenardão, E.J.; Jacob, R.G.; Panatieri, R.B. Synthesis of Vinyl Selenides. Chem. Rev. 2009, 109, 1277–1301. [CrossRef] [PubMed]
2. Perin, G.; Alves, D.; Jacob, R.G.; Barcellos, A.M.; Soares, L.K.; Lenardão, E.J. Synthesis of Organochalcogen Compounds using Non-Conventional Reaction Media. EJ ChemistrySelect 2016, 2, 205–258. [CrossRef]
3. Banerjee, B.; Koketsu, M. Recent developments in the synthesis of biologically relevant selenium containing scaffolds. Coord. Chem. Rev. 2017, 339, 104–127. [CrossRef]
4. Lenardão, E.J.; Cella, R.; Jacob, R.G.; da Silva, T.B.; Perin, G. Synthesis and Reactivity of α-Phenylseleno-β-substituted Styrenes. Preparation of (Z)-Allyl Alcohols, (E)-α-Phenyl-α,β-unsaturated Aldehydes and α-Aryl Acetophenones. J. Braz. Chem. Soc. 2006, 17, 1031–1038. [CrossRef]
5. Silveira, C.C.; Braga, A.L.; Vieira, A.S.; Zeni, G. Stereoselective Synthesis of Enynes by Nickel-Catalyzed Cross-Coupling of Divinyl Chalcogenides with Alkynes. J. Org. Chem. 2003, 68, 662–665. [CrossRef] [PubMed]
6. Silveira, C.C.; Mendes, S.R.; Wolf, L. Iron-Catalyzed Coupling Reactions of Vinylic Chalcogenides with Grignard Reagents. J. Braz. Chem. Soc. 2010, 11, 2138–2145. [CrossRef]
7. Tingoli, M.; Tecco, M.; Testaferrari, L.; Temperini, A. Alkynyl Phenyl Selenides as Convenient Precursors for the Synthesis of Stereodefined Trisubstituted Alkenes. Tetrahedron 1995, 51, 4691–4700. [CrossRef]
8. Perin, G.; Barcellos, A.M.; Luz, E.Q.; Borges, E.L.; Jacob, R.G.; Lenardão, E.J.; Sancineto, L.; Santi, C. Green Hydroselenation of Aryl Alkynes: Divinyl Selenides as a Precursor of Resveratrol. Molecules 2017, 22, 327. [CrossRef]
9. Tecco, M.; Testaferrari, L.; Temperini, A.; Bagnoli, L.; Marini, F.; Santi, C. A New Synthesis of α-Phenylseleno γ- and δ-Lactones from Terminal Alkynes. Synlett 2003, 655–668. [CrossRef]
10. Gonçalves, L.C.C.; Victória, F.N.; Lima, D.B.; Borba, P.M.Y.; Perin, G.; Savegnago, L.; Lenardão, E.J. Cul/glycerol mediated stereoselective synthesis of 1,2-bis-chalcogen alkenes from terminal alkynes: Synthesis of new antioxidants. Tetrahedron Lett. 2014, 55, 5275–5279. [CrossRef]
11. Sartori, G.; Neto, J.S.S.; Pesarico, A.P.; Back, D.F.; Nogueiraa, C.W.; Zeni, G. Bis-vinyl selenides obtained via iron(III) catalyzed addition of PhSeSePh to alkynes: Synthesis and antinociceptive activity. Org. Biomol. Chem. 2013, 11, 1199–1208. [CrossRef] [PubMed]

12. Bortolatto, C.F.; Wilhelma, E.A.; Roman, S.S.; Nogueira, C.W. (E)-2-Benzylidene-4-phenyl-1,3-diselenole ameliorates signals of renal injury induced by cisplatin in rats. J. Appl. Toxicol. 2014, 34, 87–94. [CrossRef]

13. Reddy, V.P.; Swapna, K.; Kumar, A.V.; Rao, K.R. Lanthanum-catalyzed stereoselective synthesis of vinyl sulfides and selenides. Tetrahedron Lett. 2010, 51, 293–296. [CrossRef]

14. Movassagh, B.; Mohammadi, E. Green Trends in Synthesis of Alkenyl and Alkynyl Chalcogenides. Curr. Green Chem. 2016, 3, 18–35. [CrossRef]

15. Wang, Z.; Mo, H.; Bao, W. Mild, Efficient and Highly Stereoslective Synthesis of (Z)-Vinyl Chalcogenides from Vinyl Bromides Catalyzed by Copper(I) in Ionic Liquids Based on Amino Acids. Synlett 2007, 91–94. [CrossRef]

16. Mohan, B.; Hwang, S.; Woo, H.; Park, K.H. Transition-metal free synthesis of diaryl vinyl selenides: A simple synthetic approach with high selectivity. Tetrahedron 2014, 70, 2699–2702. [CrossRef]

17. Lara, R.G.; Borges, E.L.; Lenard, E.J.; Alves, D.; Jacob, R.G.; Gelson, P. Synthesis of alkenyl selenides and tellurides using PEG-400. Arkivoc 2009, xi, 221–227. [CrossRef]

18. Lenardão, E.J.; Dutra, L.G.; Saraiva, M.T.; Jacob, R.G.; Perin, G. Hydroselelenation of alkynes using NaBH4/BMIMBF4: Easy access to vinyl selenides. Tetrahedron Lett. 2007, 48, 8011–8013. [CrossRef]

19. Soares, L.K.; Silva, R.B.; Peglow, T.J.; Silva, M.S.; Jacob, R.G.; Alves, D.; Perin, G. Selective Synthesis of Vinyl- or Alkynyl Chalcogenides from Glycerol and their Water-Soluble Derivatives. ChemistrySelect 2016, 1, 2009–2013. [CrossRef]

20. Potapov, V.A.; Elokhina, V.N.; Larina, L.I.; Yaroshenko, T.I.; Tatarinova, A.A.; Amosova, S.V. Reactions of sodium selenide with ethynyl and bromoethynyl ketones: Stereo- and regioselective synthesis of functionalized divinyl selenides and 1,3-dilene-1,1-dinitriles. J. Organomet. Chem. 2009, 694, 3679–3682. [CrossRef]

21. Knapton, D.J.; Meyer, T.Y. A Palladium-Catalyzed Regio- and Stereoselective Four-Component Coupling Reaction. J. Org. Chem. 2005, 70, 785–796. [CrossRef] [PubMed]

22. Toyofuku, M.; Fujiwara, S.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. Platinum-Catalyzed Intramolecular Vinylchalcogenation of Alkynes with β-Phenylchalcogeno Conjugated Amides. J. Am. Chem. Soc. 2008, 130, 10504–10505. [CrossRef]

23. Fujiwara, S.; Toyofuku, M.; Kuniyasu, H.; Kambe, N. Transition-metal-catalyzed cleavage of carbon–selenium bond and addition to alkynes and allenes. Pure Appl. Chem. 2010, 82, 565–575. [CrossRef]

24. Andreev, M.V.; Potapov, V.A.; Musalov, M.V.; Larina, L.I.; Amosova, S.V. Regio- and stereoselective reaction of sodium benzene-selenolate with 3-(trimethylsilyl)prop-2-ynamides. Russ. Chem. Bull. 2019, 68, 2134–2136. [CrossRef]

25. Kate, A.S.; George, S.D.; Sonawane, S.; Periyasamy, G. Nucleoside analogue as an anticancer compound. WO Patent 2013144894. Chem. Abstrs. 2013, 159, 557621.

26. Pacher, T.; Raninger, A.; Lorbeer, E.; Brecker, L.; But, P.P.-H.; Greger, H. Alcoholysis of Naturally Occurring Imides: Misleading Interpretation of Antifungal Activities. J. Nat. Prod. 2010, 73, 1389–1393. [CrossRef]

27. Moon, J.T.; Ha, S.H.; Lee, S.H.; Kwon, T.H.; Oh, C.R.; Kim, Y.D.; Kim, J.; Choo, D.J.; Lee, J.Y. Total synthesis and biological evaluation of methylgerambullone. Bioorganic Med. Chem. Lett. 2010, 20, 52–55. [CrossRef]

28. Wang, J.; Xie, L.; Wang, Y.; Wang, X.; Xi, S.; Zeng, T.; Gong, P.; Zhai, X. Design and Synthesis of Novel 4-Phenoxyquinolines Bearing 3-Hydrosulfonylcrylamido or 1H-Imidazole-4-carboxamido Scaffolds as c-Met Kinase Inhibitors. Arch. Pharm. 2017, 350, 1600307. [CrossRef]

29. Mayer, A.M.S.; Gustafson, K.R. Marine pharmacology in 2001–2: Antitumour and cytotoxic compounds. Eur. J. Cancer 2004, 40, 2676–2704. [CrossRef]
33. Huang, K.-C.; Chen, Z.; Jiang, Y.; Akare, S.; Kolber-Simonds, D.; Condon, K.; Agoulnik, S.; Tendyke, K.; Shen, Y.; Wu, K.-M.; et al. Apratoxin A Shows Novel Pancreas-Targeting Activity through the Binding of Sec 61. *Mol. Cancer Ther.* 2016, 15, 1208–1216. [CrossRef]

34. Suo, R.; Takada, K.; Irie, R.; Watanabe, R.; Suzuki, T.; Ise, Y.; Ohtsuka, S.; Okada, S.; Matsunaga, S. Poecillastrin H, a Chondropsin-Type Macrolide with a Conjugated Pentaene Moiety, from a *Characella* sp. Marine Sponge. *J. Nat. Prod.* 2018, 81, 1295–1299. [CrossRef]

35. Bezerra, D.P.; Ferreira, P.M.P.; Machado, C.M.L.; de Aquino, N.C.; Silveira, E.R.; Chammas, R.; Pessoa, C. Antitumour Efficacy of Piper tuberculatum and Pipiplartine Based on the Hollow Fiber Assay. *Planta Med.* 2015, 81, 15–19. [CrossRef]

36. Elgiushy, H.R.; Hammad, S.F.; Hassan, A.S.; Aboutaleb, N.; Abouzid, K.A.M. Acrylamide Moiety, a Valuable Fragment in Medicinal Chemistry: Insight into Synthetic Methodologies, Chemical Reactivity and Spectrum of Biological Activities of Acrylamide Derivatives. *J. Adv. Pharm. Res.* 2018, 2, 221–237. [CrossRef]

37. Lenardao, E.J.; Santi, C.; Sancineto, L. *New Frontiers in Organoselenium Compounds*; Springer International Publishing AG: Cham, Switzerland, 2018; 189p.

38. Rappoport, Z. (Ed.) *Patai’s Chemistry of Functional Groups. Organic Selenium and Tellurium Compounds*; John Wiley and Sons: Chichester, UK, 2013; Volume 4, 1678p.

39. Santi, C. (Ed.) *Organoselenium Chemistry: Between Synthesis and Biochemistry*; Bentham Science Publishers: Sharjah, UAE, 2014; 563p.

40. Woollins, J.D.; Laitinen, R.S. (Eds.) *Selenium and Tellurium Chemistry. From Small Molecules to Biomolecules and Materials*; Springer: Heidelberg, Germany, 2011; 334p.

41. Azad, G.K.; Tomar, R.S. Ebselen, a promising antioxidant drug: Mechanisms of action and targets of biological pathways. *Mol. Biol. Rep.* 2014, 41, 4865–4879. [CrossRef]

42. Back, T.G.; Dyck, B.P. A Novel Camphor-Derived Selenenamide That Acts as a Glutathione Peroxidase Mimetic. *J. Am. Chem. Soc.* 1997, 119, 2079–2083. [CrossRef]

43. Ruberte, A.C.; Sanmartin, C.; Aydillo, C.; Sharma, A.K.; Plano, D. Development and Therapeutic Potential of Selenazo Compounds. *J. Med. Chem.* 2020, 63, 1473–1489. [CrossRef]

44. Yu, S.-C.; Kuhn, H.; Daniliuc, C.-G.; Ivanov, I.; Jones, P.G.; du Mont, W.-W. 5-Selenization of salicylic acid derivatives yielded isoform-specific 5-lipoxygenase inhibitors. *Org. Biomol. Chem.* 2010, 8, 828–834. [CrossRef]

45. Braverman, S.; Cherkinsky, M.; Kalendar, Y.; Jana, R.; Sprecher, M.; Goldberg, I. Synthesis of water-soluble vinyl selenides and their high glutathione peroxidase (GPx)-like antioxidant activity. *Synthesis* 2014, 46, 119–125. [CrossRef]

46. Back, T.G.; Moussa, Z. Remarkable Activity of a Novel Cyclic Seleninate Ester as a Glutathione Peroxidase Mimetic and Its Facile in Situ Generation from Allyl 3-Hydroxypropyl. *J. Am. Chem. Soc.* 2003, 125, 13455–13460. [CrossRef] [PubMed]

47. Gusarova, N.K.; Potapov, V.A.; Amosova, S.V.; Trofimov, B.A. Alkylvinyl Selenides from Acetylene, Elemental Selenium and Alkyl Halides. *Zhurnal Org. Khimii* 1983, 19, 2477–2480. (In Russian)

48. Gusarova, N.K.; Potapov, V.A.; Amosova, S.V.; Sinegovskaya, L.M. Reactions of Elemental Selenium with Alkynes. 1. Identification of Products of Reaction of Elemental Selenium with Acetylene. *Zhurnal Org. Khimii* 1984, 20, 484–489. (In Russian)

49. Potapov, V.A.; Gusarova, N.K.; Amosova, S.V.; Kashik, A.S.; Trofimov, B.A. Reactions of Chalcogen with Acetylene. *Zhurnal Org. Khimii* 1986, 22, 276–281. (In Russian)

50. Rusakov, Y.Y.; Krivdin, L.B.; Istomina, N.V.; Potapov, V.A.; Amosova, S.V. Conformational study and stereochemical behavior of its $^{77}$ Se-$^1$ H spin-spin coupling constants. *Magn. Reson. Chem.* 2008, 46, 979–985. [CrossRef]

51. Musalov, M.V.; Potapov, V.A.; Amosova, S.V. Reaction of diselenium dichloride with acetylene. *Russ. J. Org. Chem.* 2011, 47, 1115–1116. [CrossRef]
54. Potapov, V.A.; Musalov, M.V.; Khuriganova, O.I.; Larina, L.I.; Amosova, S.V. Reactions of stereoselective addition of selenium dibromide and monobromide to acetylene. *Russ. J. Org. Chem.* **2010**, *46*, 753–754. [CrossRef]

55. Potapov, V.A.; Khuriganova, O.I.; Musalov, M.V.; Larina, L.I.; Amosova, S.V. Stereospecific synthesis of E,E-bis(2-chlorovinyl)selenide. *Russ. J. Gen. Chem.* **2010**, *80*, 541–542. [CrossRef]

56. Musalov, M.V.; Potapov, V.A.; Musalova, M.V.; Amosova, S.V. Stereoselective synthesis of (E,E)-bis(2-halovinyl) selenides and its derivatives based on selenium halides and acetylene. *Tetrahedron* **2012**, *68*, 10567–10572. [CrossRef]

57. Potapov, V.A.; Ishigeev, R.S.; Amosova, S.V.; Borodina, T.N. Synthesis of a novel family of water-soluble 2H,3H-[1,3]thia-and -selenazo[3,2-alpyridin-4-ium heterocycles by annulation reactions. *Tetrahedron Lett.* **2019**, *60*, 475–479. [CrossRef]

58. Medvedeva, A.S. Effect of a Heteroatom on the Reactivity of Silicon and Germanum Acetilenic Alcohols, Ethers, and Carbonyl Compounds. *Russ. J. Org. Chem.* **1996**, *32*, 272–287. (In Russian)

59. Potapov, V.A. Organic diselenides, ditellurides, polyselenides and polytellurides. Synthesis and reactions. In Patai’s *Chemistry of Functional Groups. Organic Selenium and Tellurium Compounds*; Rappoport, Z., Ed.; John Wiley and Sons, Inc.: Chichester, UK, 2013. [CrossRef]

60. Andreev, M.V.; Safronova, L.P.; Medvedeva, A.S. Highly Efficient Desilylation of 3-Trimethylsilylprop-2-ynamides by the Action of KF–Al2O3. *Russ. J. Org. Chem.* **2011**, *47*, 1797–1801. [CrossRef]

61. Medvedeva, A.S.; Andreev, M.V.; Safronova, L.P. One-Pot Synthesis of 3-(Trimethylsilyl)propynamides. *Russ. J. Org. Chem.* **2010**, *46*, 1466–1470. [CrossRef]

62. Demina, M.M.; Velikanov, A.A.; Medvedeva, A.S.; Larina, L.I.; Voronkov, M.G. Universal method for trimethylsilylation of acetylenic alcohols and glycols. *J. Organomet. Chem.* **1998**, *553*, 129–133. [CrossRef]

63. Medvedeva, A.S.; Novokshonov, V.V.; Demina, M.M.; Voronkov, M.G. An unusual rearrangement of 1-trimethylsiloxy-3-bromomagnesium-2-propyne. *J. Organomet. Chem.* **1998**, *553*, 481–482. [CrossRef]

64. Andreev, M.V.; Medvedeva, A.S.; Larina, L.I.; Demina, M.M. Synthesis of 5-aminoisoxazoles from 3-trimethylsilylprop-2-ynamides. *Mendeleev Commun.* **2017**, *27*, 175–177. [CrossRef]

65. Mareev, A.V.; Andreev, M.V.; Ushakov, I.A. Base-Catalyzed Hydration of Silicon-Containing Activated Alkynes: The Effect of Substituents at the Triple Bond. *ChemistrySelect* **2020**, *5*, 10736–10742. [CrossRef]

66. Andreev, M.V.; Safronova, L.P.; Medvedeva, A.S. Efficient Tandem Synthesis of 3-Alkylaminoprop-2-enamides from 3-trimethylsilylprop-2-ynamide. *Russ. J. Org. Chem.* **2013**, *49*, 822–827. [CrossRef]

**Sample Availability:** Samples of the compounds are not available from the authors.

**Publisher’s Note:** MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

© 2020 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).