

# An alternative approach to selenides and diselenides from Se(0) and epoxides/aziridines under sustainable conditions

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Dedicated to Professor Jozef Drabowicz on the occasion of his 76th birthday

Received mm-dd-yyyy

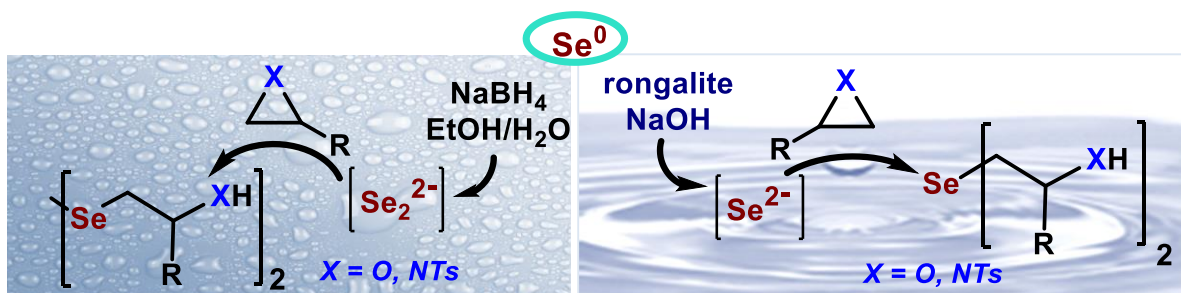
Accepted Manuscript mm-dd-yyyy

Published on line mm-dd-yyyy

Dates to be inserted by editorial office

## Abstract

The *on-water* reduction of elemental selenium promoted by rongalite (sodium hydroxymethanesulfinate)/sodium hydroxide provided selenide anions, which led to a variety of  $\beta$ -hydroxy and  $\beta$ -amino selenides upon reaction with epoxides and aziridines through an alternative and sustainable approach. The reactions are operationally simple and occur in a highly regioselective and enantioconservative way. The preparation of diselenides was also accomplished by a different approach which relies on the generation of diselenide dianions from elemental selenium and sodium borohydride. Reaction with three-membered heterocycles led to differently substituted  $\beta$ -hydroxy and  $\beta$ -amino diselenides.



**Keywords:** Selenides, diselenides, *on-water* reactions, rongalite, sodium borohydride

## Introduction

Organoselenium derivatives are involved in many useful synthetic transformations.<sup>1-3</sup> Diselenides, selenides and selenols are widely used to introduce seleno moieties into organic structures.<sup>4-9</sup> Selenated molecules also represent a class of compounds with various applications in biology, medicine,<sup>10</sup> for example as antioxidants,<sup>11,12</sup> enzyme modulators<sup>13-15</sup> and anticancer agents,<sup>16-19</sup> and in materials chemistry.<sup>20,21</sup>

During the course of our studies on chalcogenated systems we reported a convenient methodology to prepare diorganyl selenides and diselenides bearing on a  $\beta$ -position hydroxy, mercapto and amino groups.<sup>22</sup> The synthetic procedure was based on the ring opening of epoxides, thiiranes and aziridines by bis(trimethylsilyl)selenide (HMDSS) under fluoride ion or phenoxide ion<sup>23</sup> catalysis. Furthermore,  $\beta$ -substituted selenols were also prepared from HMDSS and three-membered heterocycles under strictly controlled conditions.<sup>24</sup>

In this context, a search for new and alternative methods to synthesize selenated organic molecules is of increasing interest, particularly when mild and sustainable reaction conditions are employed.

We recently found that the preparation of another class of chalcogen-containing organic molecules, such as tellurides and ditellurides, could be accomplished using a rongalite<sup>25</sup> (sodium hydroxymethanesulfinate)-promoted *on-water* procedure to generate tellurium nucleophilic species, followed by their reaction with various electrophiles, such as strained heterocycles, alkyl bromides and Michael acceptors.<sup>26</sup> Rongalite was demonstrated as an efficient reducing agent to prepare Na<sub>2</sub>Te from Te(0) in aqueous NaOH. The reaction was carried out at 80 °C for one hour and then reacted with the electrophile.

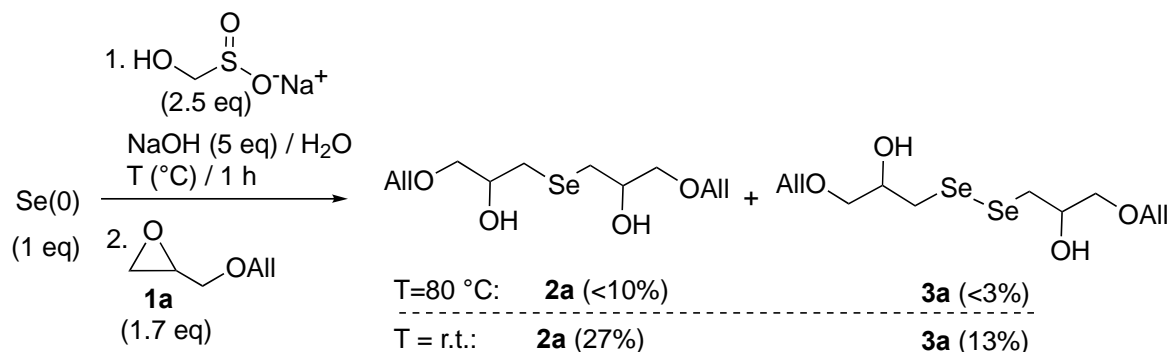
Indeed, only one example for the preparation of 1,1'-selenobis(propan-2-ol) by the treatment of epoxyp propane with rongalite/sodium hydroxide had been reported.<sup>27</sup>

On the basis of these considerations and taking into account the interest in selenium-containing molecules, we describe here an alternative procedure to synthesise a representative series of  $\beta$ -substituted selenides through the *on-water* reaction of Na<sub>2</sub>Se with epoxides and aziridines.  $\beta$ -Functionalized diselenides were also prepared by means of a suitably modified approach with sodium borohydride in ethanolic aqueous solution.

## Results and Discussion

Initially, our attention was addressed to evaluating whether the above described method for the preparation of tellurides and ditellurides<sup>26</sup> could be extended to prepare the selenated analogues. This approach would provide an alternative route, economically and environmentally more convenient with respect to the previously reported methodologies.

Firstly, elemental selenium (1 eq.), rongalite (2.5 eq.) and sodium hydroxide (5 eq.) were heated at 80 °C in water for 1 h, to generate Na<sub>2</sub>Se under *on-water* conditions. However, after the addition of the epoxide **1a** (1.7 eq.) a complex mixture of products was observed, containing the selenide **2a** in very low yield (<10%), together with traces of the diselenide **3a**, as well as of polyselenated compounds and unreacted epoxide (Scheme 1).



Scheme 1

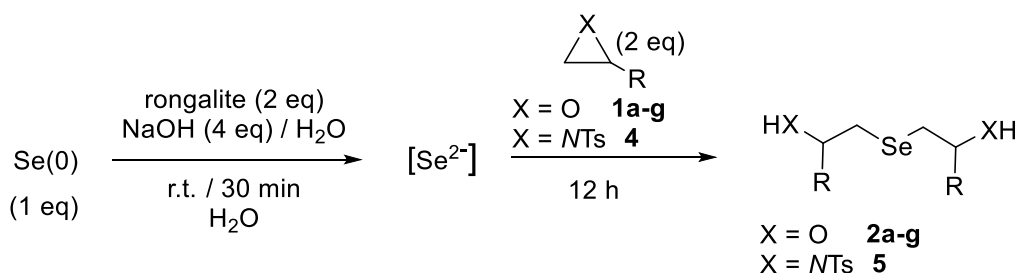
This result showed that the reaction conditions used for the synthesis of tellurium derivatives cannot be directly applied to obtain selenides.

Taking into account that the reduction potential of selenium is lower than that of tellurium,<sup>28</sup> milder conditions were then used to generate the selenated dianionic reagent ( $\text{Se}^{2-}$ ).  $\text{Se}(0)$  was treated at room temperature in water for 1 h with rongalite and  $\text{NaOH}$ , and an orange solution was produced. After addition of the epoxide **1a** the formation of both selenide **2a** and diselenide **3a** was observed, in the ratio 2:1 (Scheme 1), together with unreacted epoxide (ca. 30%).

This result, although not providing a selective entry to the desired compounds, is of itself rather interesting, as it allowed one to observe for the first time the formation of a selenide, and of a diselenide, under rongalite-promoted *on-water* conditions through the nucleophilic ring opening of epoxides by  $\text{Se}^{2-}$  anions.

With the aim to have better selectivity, the reaction was carried out changing the conditions (reaction time, amount of the reducing system and of the epoxide). After optimization, it was observed that the treatment, under inert atmosphere, of elemental selenium in water with 2.0 eq. of rongalite, 4 eq. of sodium hydroxide at r.t. for 30 min., led to a white-yellowish solution, which indicated the formation of  $\text{Na}_2\text{Se}$ . The reaction mixture turned to dark yellow upon addition of the epoxide **1a** (2 eq.). After stirring overnight, under these conditions the selenide **2a** was obtained as the main product (Table 1, entry 1). To evaluate the generality of this procedure, differently substituted epoxides, including glycidol derivatives and eugenol epoxide, were reacted, providing the corresponding  $\beta$ -hydroxy selenides **2b-g** in good yields, as mixture of diastereoisomers. The results are summarized in Table 1, entries 2-8.

**Table 1.** Synthesis of  $\beta$ -substituted selenides **2**, **5** by rongalite-promoted *on-water*  $\text{Se}(0)$  reduction and reaction with epoxides **1** and aziridines **4**



Entry	X	R	Product	Yield <sup>a,b</sup>
1	O	CH <sub>2</sub> OAll	<b>2a</b>	69%
2	O	CH <sub>2</sub> O <sup>i</sup> Pr	<b>2b</b>	68%
3	O	CH <sub>2</sub> OBn	<b>2c</b>	83%
4	O	( <i>R</i> )-CH <sub>2</sub> OBn	(2 <i>S</i> , 2' <i>S</i> )- <b>2c</b>	76%
5	O	CH <sub>2</sub> Cl	<b>2d<sup>c</sup></b> (R=Me)	62%
6	O	CH <sub>2</sub> CH <sub>3</sub>	<b>2e</b>	77%
7	O	-(CH <sub>2</sub> ) <sub>4</sub> -	<b>2f</b>	49%
8	O	CH <sub>2</sub> [2-methoxy-phenyl acetate]	<b>2g</b>	70%
9	<i>N</i> -Ts	( <i>S</i> )-CH <sub>3</sub>	(2 <i>S</i> , 2' <i>S</i> )- <b>5</b>	58%
10	<i>N</i> -Ts	( <i>R</i> )-CH <sub>3</sub>	(2 <i>R</i> , 2' <i>R</i> )- <b>5</b>	61%

<sup>a</sup>Yields refer to both diastereoisomers. <sup>b</sup>Minor amounts of the corresponding diselenide were observed (ca. 10%). <sup>c</sup>Selenide **2d** [CH<sub>3</sub>CH(OH)CH<sub>2</sub>]<sub>2</sub>Se was obtained.

The reaction conditions are operationally simple and show good yields in the case of monosubstituted epoxides (Table 1, entries 1-4, 6, 8), while with the disubstituted oxirane **1f**, a lower yield was observed (Table 1, entry 7). It is important to point out that under these conditions the protecting groups on the side-chain of glycidol derivatives were maintained. Of particular interest is the hydroxy selenide **2g** arising from a natural product, such as eugenol (Table 1, entry 8).

When epichlorohydrin **1d** was employed, the β-hydroxy selenide **2d** [CH<sub>3</sub>CH(OH)CH<sub>2</sub>]<sub>2</sub>Se, bearing a methyl group instead of the chloromethyl moiety, was achieved (Table 1, entry 5). As observed for the related tellurenylation route,<sup>26</sup> the formation of **2d** can be rationalized through the ring opening of the epoxide by the nucleophilic species (Se<sup>2-</sup>) and a selenium-mediated halogenophilic reaction (S<sub>N</sub>2Hal).

Furthermore, similarly to what was observed in the ring opening of epoxides by HMDSS, a regioselective attack by the nucleophilic selenium species on the less substituted side of the heterocycle was always observed, leading to β-disubstituted compounds **2a-g**.

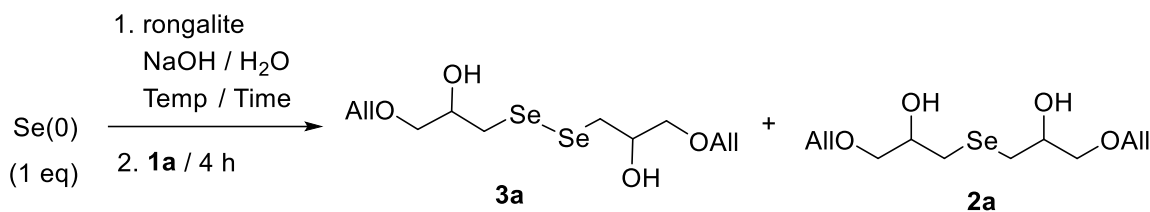
These conditions were also efficiently applied for the ring opening of aziridines by the selenated dianion (Se<sup>2-</sup>). *N*-Tosyl aziridines (*S*)-**4** and (*R*)-**4**, prepared from the natural and non-natural amino acid L- and D-alanine, led to the enantiomeric pair of β-amino selenides (2*S*, 2'*S*)-**5** and (2*R*, 2'*R*)-**5** (Table 1, entries 9, 10).

As a further step, taking into account that in the synthesis of **2a** we also observed the formation of the diselenide **3a** (Scheme 1), we were interested in exploring the conditions to prepare selectively diselenides from elemental selenium and rongalite/sodium hydroxide. Using the optimized conditions for the reduction of Se(0), the amount of the epoxide **1a** was initially reduced to 0.4 eq, in order to avoid, or minimize, the attack of the intermediate nucleophile (RSe<sup>-</sup>) on a second molecule of **1a**. Nevertheless, the selenide **2a** was again the major reaction product, and the diselenide **3a** was observed in only very low yield (<10%) (Table 2, entry 1). This result highlights that the formation of the diselenide by oxidation of (RSe<sup>-</sup>) intermediates is difficult under these conditions.

We then decided to search for different conditions to generate (Se<sub>2</sub><sup>2-</sup>) from Se(0)/rongalite/NaOH/H<sub>2</sub>O, to be reacted with the epoxide. For this purpose we diminished the amount of the reducing system, aiming to

avoid the formation of the ( $\text{Se}^{2-}$ ) species and favour that of ( $\text{Se}_2^{2-}$ ). Therefore, the reaction was performed under various conditions, as reported in Table 2 (entries 2-7).

**Table 2.** Search for reaction conditions to synthesize diselenides **3**



Entry	Rongalite	NaOH	Temp	Time	<b>1a</b>	<b>3a</b> : <b>2a</b> <sup>a</sup>	Yield <sup>b,c</sup>
1	2 eq	4 eq	r.t.	30 min	0.4 eq	<1 : 10	27%
2	2.5 eq	5 eq	r.t.	1 h	0.4 eq	<1 : 10	41% <sup>d</sup>
3	1 eq	2 eq	r.t.	1 h	0.8 eq	1 : 3	30%
4	0.5 eq	1 eq	r.t.	1 h	0.8 eq	1 : 2	24%
5	0.5 eq	1 eq	90 °C	1 h	0.8 eq	1 : 3	20% <sup>d</sup>
6	0.4 eq	0.8 eq	r.t.	1 h	0.6 eq	1 : 2	32%
7	0.4 eq	0.8 eq	r.t.	1 h	0.6 eq <sup>e</sup>	1 : 1.5	44%

<sup>a</sup>Ratio determined by  $^1\text{H}$ -NMR. <sup>b</sup>Total yield (determined by NMR). <sup>c</sup>Ca. 30%-40% of unreacted epoxide was recovered. <sup>d</sup>Polyselenated side products were observed. <sup>e</sup>Addition of the epoxide at 0 °C.

As can be observed, neither variation of the ratio nor the temperature, nor the time enabled us to obtain the desired diselenide **3a** as the sole, or the major product. Significant amounts of the selenide **2a** were always formed, together with polyselenated side products and unreacted epoxide. The possibility to generate  $\text{Na}_2\text{Se}_2$  upon disproportionation of  $\text{Na}_2\text{Se}$  (prepared from  $\text{Se}(0)$  and rongalite) and elemental selenium was also investigated.<sup>26</sup> However, when the reaction mixture was treated with the epoxide **1a**, comparable amounts of selenide **2a** and diselenide **3a** were again observed.

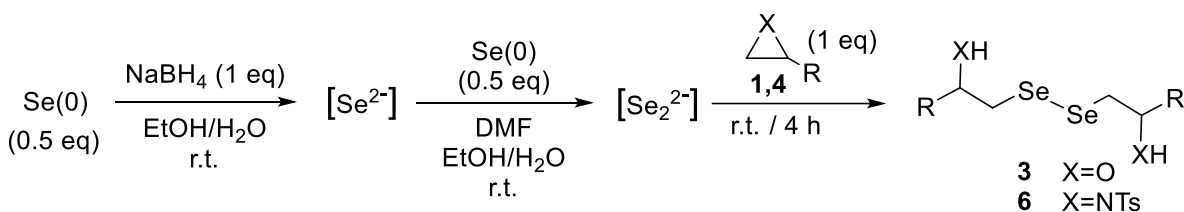
Our attention was then turned towards the search of a different approach to generate  $\text{Na}_2\text{Se}_2$ . Several methods are reported to reduce elemental selenium to diselenide dianions, such as treatment with superhydride ( $\text{LiEt}_3\text{BH}$ ),<sup>29</sup> sodium hydride,<sup>30</sup> sodium borohydride<sup>31</sup> and hydrazine.<sup>32,33</sup>

With the aim of using a mild and possibly sustainable approach, elemental selenium was reduced by means of a slightly modified reported procedure.<sup>34</sup>  $\text{Se}(0)$  (0.5 eq.) was treated with sodium borohydride (1 eq.) in aqueous ethanol solution (80%), at room temperature under an inert atmosphere. A change of the colour was observed from dark red to colourless. Then DMF and an 80% solution of  $\text{EtOH}/\text{H}_2\text{O}$  were added (red brownish colour), and the mixture was stirred until gas evolution ended. After that, it was treated with additional elemental selenium (0.5 eq) and stirred at room temperature for 90 min. A dark reddish solution of  $\text{Na}_2\text{Se}_2$  was obtained, and the epoxide **1a** (1 eq) was then added *in situ* and the mixture stirred overnight. Under these conditions, the desired diselenide **3a** was actually formed as major compound in good yield (Table 3, entry 1). This procedure was applied to differently substituted epoxides, leading to diselenides **3**,

arising from a regioselective attack of the nucleophile on the less substituted side of the three-membered ring. Results are reported in Table 3 (entries 1-8).

(*R*)-2-Methyl-*N*-tosylaziridine (*R*)-**4** was also reacted with the selenide dianion, providing the corresponding enantiopure diselenide (2*R*,2'*R*)-**6** (Table 3, entry 9).

**Table 3.** Synthesis of diselenides from (Na<sub>2</sub>Se<sub>2</sub>) and epoxides **1** or aziridine **4**



Entry	X	R	Product	Yield <sup>a</sup>
1	O	CH <sub>2</sub> OAll	<b>3a</b>	62%
2	O	CH <sub>2</sub> O <sup>i</sup> Pr	<b>3b</b>	68%
3	O	CH <sub>2</sub> OBn	<b>3c</b>	83%
4	O	( <i>R</i> )-CH <sub>2</sub> OBn	(2 <i>S</i> ,2' <i>S</i> )- <b>3c</b>	76%
5	O	CH <sub>2</sub> CH <sub>3</sub>	<b>3e</b>	71%
6	O	-(CH <sub>2</sub> ) <sub>4</sub> -	<b>3f</b>	52%
8	O	CH <sub>2</sub> NPhth	<b>3h</b>	24%
9	<i>N</i> -Ts	( <i>R</i> )-CH <sub>3</sub>	(2 <i>R</i> ,2' <i>R</i> )- <b>6</b>	55%

<sup>a</sup>Yields refer to both diastereoisomers

## Conclusions

In conclusion, we have devised an alternative procedure to obtain differently substituted β-hydroxy and β-amino selenides through *on-water* reaction of sodium selenide and three-membered heterocycles. The use of rongalite/NaOH as a convenient and water soluble reducing system allowed the selenides to be prepared under sustainable conditions. The β-functionalized diselenides were also prepared by a different procedure to generate sodium diselenide with sodium borohydride in aqueous ethanol solution, to be reacted with epoxides and aziridines.

## Experimental Section

**General.** All commercial materials were used as received, without further purification. Flash column chromatography purifications were performed with Silica gel 60 (230-400 mesh). Thin layer chromatography was performed with TLC plates Silica gel 60 F<sub>254</sub>, which was visualised under UV light, or by staining with an

ethanolic acid solution of *p*-anisaldehyde followed by heating. Reactions were performed in water. Mass spectra were determined by electron ionization (EI, 70 eV) or by Electrospray Ionization (ESI).  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded in  $\text{CDCl}_3$  using a Varian 200 spectrometers operating at 200 MHz or 400 MHz or a Bruker 400 Ultrashield spectrometer operating at 400 MHz (for  $^1\text{H}$ ) and 50 or 100 MHz (for  $^{13}\text{C}$ ). NMR signals were referenced to non deuterated residual solvent signal 7.26 ppm for  $^1\text{H}$ , and 77.0 ppm, central line of  $\text{CDCl}_3$ , for  $^{13}\text{C}$ . Chemical shifts ( $\delta$ ) are given in parts per million (ppm), and coupling constants ( $J$ ) are given in Hertz (Hz), rounded to the nearest 0.1 Hz. Multiplicity is reported as: s = singlet, d = doublet, t = triplet, ap d = apparent doublet, m = multiplet, dd = doublet of doublet, bs = broad singlet, bd = broad doublet. For known compounds, all the spectroscopic data matched those reported in the literature. Non commercially available epoxide **1g**<sup>35</sup> and *N*-Ts-aziridines **4**<sup>36</sup> were synthesized following reported procedures.

### General procedure for the synthesis of $\beta$ -hydroxy-selenides (**2**) and $\beta$ -amino-selenides (**5**).

Elemental selenium (79 mg, 1.0 mmol, 1 eq.), sodium hydroxymethanesulfinate dihydrate (308 mg, 2.0 mmol, 2.0 eq.) and NaOH (160 mg, 4.0 mmol, 4.0 eq.) were placed in a 10mL vial with 2 mL of water. The vial was sealed and the reaction mixture was stirred for 30 min at rt under an inert atmosphere. The colour of the solution turned from red to light orange-yellowish. The epoxide, or the aziridine, (1.7 mmol, 1.7 eq.) was then added, and the reaction mixture was stirred at rt for additional 4 h. Afterwards, the mixture was treated with saturated aq.  $\text{NH}_4\text{Cl}$  (2 mL) and EtOAc (5 mL) was added. The aqueous phase was extracted with EtOAc (2 x 5 mL), and the combined organic phases were dried over  $\text{Na}_2\text{SO}_4$ . The solvent was evaporated under vacuum to afford a crude product, which was purified on silica gel chromatography.

**3,3'-Selenobis(1-(allyloxy)propan-2-ol) (2a).** Yellow oil, yield 69% (PE/EtOAc 2:1,  $R_f$  = 0.65; mixture of diastereoisomers). Spectroscopic data matched those previously reported.<sup>21</sup>  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm): 2.61–2.89 (m, 12 H), 3.40–3.59 (m, 8 H), 3.90–3.99 (m, 4 H), 4.00–4.09 (m, 8 H), 5.12–5.38 (m, 8 H), 5.79–6.00 (m, 4 H) ppm.  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 28.9, 70.0, 70.1, 72.3, 76.4, 117.3, 134.3. MS:  $m/z$  (%) = 253 (6), 97 (24), 57 (14), 55 (15), 41 (100).

**3,3'-Selenobis(1-isopropoxypropan-2-ol) (2b).** Pale yellow oil, yield 68% (PE/EtOAc 3:1,  $R_f$  = 0.74; mixture of diastereoisomers). Spectroscopic data matched those previously reported.<sup>21</sup>  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 1.15 (d,  $J$  6.2 Hz, 24 H), 2.70 (dd,  $J$  6.2, 12.8 Hz, 4 H), 2.71 (dd,  $J$  6.8, 12.8 Hz, 4 H), 2.81 (bs, 4H), 3.39–3.44 (m, 4 H), 3.45–3.50 (m, 4 H), 3.53–3.66 (m, 4 H), 3.86–3.93 (m, 4 H).  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 22.0, 28.7, 70.0, 70.3, 71.2, 72.2.

**3,3'-Selenobis(1-(benzyloxy)propan-2-ol) (2c).** Yellow oil, yield 83% (PE/EtOAc 2:1,  $R_f$  = 0.7; mixture of diastereoisomers). Spectroscopic data matched those previously reported.<sup>21</sup>  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 2.71 (dd,  $J$  = 7.2, 12.8 Hz, 4 H), 2.81 (dd,  $J$  = 4.8, 12.8 Hz, 4 H), 3.15 (bs, 4 H), 3.40–3.60 (m, 8 H), 3.90–4.00 (m, 4 H), 4.55 (ap s, 8 H), 7.20–7.40 (m, 20 H).  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 28.9, 70.0, 70.1, 73.2, 73.4, 127.7, 128.4, 137.7.

**(2S,2'S)-3,3'-Selenobis(1-(benzyloxy)propan-2-ol) [(2S,2'S)-2c].** Yellow oil, yield 76%. Spectroscopic data matched those previously reported.<sup>21</sup> (PE/EtOAc 2:1,  $R_f$  = 0.7).  $[\alpha]_{\text{D}}^{20}$  = -61 ( $c$  = 0.3,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) = 2.71 (dd,  $J$  7.0, 12.8 Hz, 2 H), 2.82 (dd,  $J$  4.8, 12.8 Hz, 2 H), 3.06 (bs, 2 H), 3.48–3.60 (m, 4 H), 3.91–4.06 (m, 2 H), 4.55 (ap s, 4 H), 7.27–7.41 (m, 10 H).

**1,1'-Selenobis(propan-2-ol) (2d).** Pale yellow oil, yield 62% (PE/EtOAc 3:1,  $R_f$  = 0.8; mixture of diastereoisomers). Spectroscopic data matched those previously reported.<sup>35</sup>  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 1.26 (d,  $J$  6.2 Hz, 12 H), 2.56–2.63 (4H, m), 2.78–2.83 (4H, m), 2.88 (bs, 4 H), 3.87–3.95 (m, 4 H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 22.7, 22.8, 34.8, 35.0, 66.6, 67.1. MS (EI):  $m/z$  (%) = 197 (3) [ $\text{M}^+$ ], 180 (100), 153 (42), 139 (16).

**1,1'-Selenobis(butan-2-ol) (2e).** Pale yellow oil, yield 77% (PE/EtOAc 3:1,  $R_f$  = 0.72; mixture of diastereoisomers).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm): 0.96 (t,  $J$  7.4 Hz, 12H), 1.52–1.59 (m, 8H), 2.59 (dd,  $J$  5.3, 7.7 Hz, 2H), 2.62 (dd,  $J$  5.3, 7.7 Hz, 2H), 2.73 (bs, 4H), 2.83 (dd,  $J$  1.8, 3.3 Hz, 2H), 2.86 (dd,  $J$  1.8, 3.3 Hz, 2H), 3.62–3.66 (m, 4H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm): 10.1, 29.7, 29.8, 33.0, 33.3, 71.8, 72.3.

**2,2'-Selenobis(cyclohexan-1-ol) (2f).**<sup>37</sup> Light yellow oil, yield 49% (PE/EtOAc 3:1,  $R_f$  = 0.83; mixture of diastereoisomers).  $^1\text{H}$ -NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 1.27–1.40 (m, 12H), 1.46–1.95 (m, 12H), 2.12–2.33 (m, 8H), 2.57–3.10 (m, 8H), 3.35–3.64 (m, 4H).  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 25.1, 26.5, 26.9, 27.2, 34.6, 4, 35.1, 47.7, 48.2, 71.6, 73.7. MS (ESI, negative):  $m/z$  = 276  $[\text{M-H}]^-$ .

**(Selenobis(2-hydroxypropane-3,1-diyl))bis(2-methoxy-4,1-phenylene) diacetate (2g).** Pale yellow solid, yield 70% (PE/EtOAc 1:1; mixture of diastereoisomers). Spectroscopic data matched those previously reported.<sup>21</sup>  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 2.30 (s, 12 H), 2.62–2.97 (m, 20 H), 3.80 (s, 12 H), 3.88–4.02 (m, 4 H), 6.62–6.88 (m, 8 H), 6.94 (ap d,  $J$  7.6 Hz, 4 H) ppm.  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 20.7, 32.5, 43.2, 55.8, 71.9, 72.1, 113.5, 121.4, 122.6, 136.8, 138.3, 150.8, 169.1.

***N,N'*-[(2*S*,2'*S*)-Selenobis(2-methylpropane-3,1-diyl)]bis(4-methylbenzenesulfonamide) [(2*S*,2'*S*)-5].** Light yellow solid, yield 58% (PE/EtOAc 3:1,  $R_f$  = 0.38).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm): 1.04 (d,  $J$  6.6 Hz, 6H), 2.40 (s, 6H), 2.47–2.55 (m, 4H), 3.36–3.42 (m, 2H), 5.17 (d,  $J$  7.0 Hz, 2H), 7.28 (ap d,  $l_s$  = 8.1 Hz, 4H), 7.75 (ap d,  $l_s$  = 8.1 Hz, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 21.2, 21.5, 33.0, 49.6, 127.1, 129.7, 137.8, 143.4. MS (ESI, negative):  $m/z$  = 502  $[\text{M-H}]^-$ .

***N,N'*-[(2*R*,2'*R*)-Selenobis(2-methylpropane-3,1-diyl)]bis(4-methylbenzenesulfonamide) [(2*R*,2'*R*)-5].** Light yellow solid, yield 61% (PE/EtOAc 3:1,  $R_f$  = 0.4).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm): 1.04 (d,  $J$  6.6 Hz, 6H), 2.40 (s, 6H), 2.47–2.55 (m, 4H), 3.36–3.42 (m, 2H), 5.17 (d,  $J$  7.0 Hz, 2H), 7.28 (ap d,  $l_s$  = 8.1 Hz, 4H), 7.75 (ap d,  $l_s$  = 8.1 Hz, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 21.2, 21.5, 33.0, 49.6, 127.1, 129.7, 137.8, 143.4.

**General procedure for the synthesis of  $\beta$ -hydroxy-diselenides (3) and  $\beta$ -amino-diselenides (6).** Elemental selenium (79 mg, 1.0 mmol, 1.0 eq.) in EtOH (2 mL) (80% aqueous solution) was added with sodium borohydride (76 mg, 2.0 mmol, 1.0 eq.) at rt. The mixture was stirred until the reagents dissolved (the colour turned from dark-red to whitish). Then, DMF (1.5 mL) (brownish-red colour) and EtOH (1 mL, 80% aq. solution) were added. The solution was stirred until gas evolution ceased, and additional 79 mg (1 mmol) of elemental selenium were added (dark-red solution). After stirring 1.5 hour at rt, the epoxide, or the aziridine, (1.0 eq.) was added and the reaction mixture was stirred for additional 4 h. The mixture was then treated with  $\text{Et}_2\text{O}$  (2 mL) and a saturated aq.  $\text{NH}_4\text{Cl}$  (3 mL). The organic phase was washed with brine (2 x 2 mL) and dried over  $\text{Na}_2\text{SO}_4$ . After evaporation of the solvent under vacuum, the crude product was purified on silica gel (typically: hexanes/EtOAc 1:1 or 2:1).

**3,3'-Diselanediylbis(1-(allyloxy)propan-2-ol) (3a).** Yellow oil, yield 63% (PE/EtOAc 2:1,  $R_f$  = 0.74; mixture of diastereoisomers). Spectroscopic data matched those previously reported.<sup>21</sup>  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 2.63 (bs, 4 H), 3.09 (dd,  $J$  12.8, 7.2 Hz, 4 H), 3.16 (dd,  $J$  12.8, 5.2 Hz, 4 H), 3.44–3.58 (m, 8 H), 4.02–4.06 (m, 12 H), 5.21–5.31 (m, 8 H), 5.82–5.96 (m, 4 H).  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 28.9, 34.0, 35.7, 69.7, 70.2, 72.4, 72.9, 73.2, 117.4, 134.3. MS (EI):  $m/z$  (%) = 390 (1)  $[\text{M}^+]$ , 195 (7), 97 (12), 57 (26), 43 (21), 41 (100), 39 (13).

**3,3'-Diselanediylbis(1-isopropoxypropan-2-ol) (3b).** Yellow oil, yield 68% (PE/EtOAc 1:1,  $R_f$  = 0.8; mixture of diastereoisomers). Spectroscopic data matched those previously reported.<sup>21</sup>  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 1.17 (d,  $J$  6.0 Hz, 12 H), 1.16 (d,  $J$  6.0 Hz, 12 H), 2.47 (br. s, 4 H), 3.06–3.19 (m, 4 H), 3.40–3.66 (m, 16 H),



3.85-3.91 (m, 2 H), 3.94-4.03 (m, 2 H).  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 22.1, 34.1, 70.3, 70.9, 71.2, 72.2, 72.3. MS (EI):  $m/z$  (%) = 394, (3)  $[\text{M}^+]$ , 99 (19), 75 (42), 73 (15), 59 (6), 57 (75), 43 (100).

**3,3'-Diselanediylbis(1-(benzyloxy)propan-2-ol) (3c).** Yellow oil, yield 83% (PE/EtOAc 2:1,  $R_f$  = 0.7; mixture of diastereoisomers). Spectroscopic data matched those previously reported.<sup>21</sup>  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 2.65 (bs, 4 H), 3.06-3.22 (m, 8 H), 3.44-3.61 (m, 8 H), 4.01-4.09 (m, 4 H), 4.56 (m, 8H), 7.28-7.39 (m, 20 H).  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 34.1, 70.2, 72.9, 73.5, 127.6, 127.7, 128.3, 137.6. MS (EI):  $m/z$  (%) = 488 (1)  $[\text{M}^+]$ , 244 (52), 91 (100).

**(2S,2'S)-3,3'-Diselanediylbis(1-(benzyloxy)propan-2-ol) [(2S,2'S)-3c].** Yellow oil, yield 76% (PE/EtOAc 2:1,  $R_f$  = 0.7).  $[\alpha]_{\text{D}}^{20}$  = -82 ( $c$  = 0.25,  $\text{CHCl}_3$ ). Spectroscopic data matched those previously reported.<sup>21</sup>  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 2.40 (bs, 2 H), 3.09 (dd,  $J$  4.8, 12.8 Hz, 2H), 3.16 (dd,  $J$  7.6, 12.8 Hz, 2 H), 3.50-3.62 (m, 4 H), 4.01-4.12 (m, 2 H), 4.56 (ap s, 4 H), 7.30-7.36 (m, 10H).

**1,1'-Diselanediylbis(butan-2-ol) (3e)** Light yellow oil, yield 71% (PE/EtOAc 3:1,  $R_f$  = 0.8; mixture of diastereoisomers).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 200 MHz)  $\delta$  (ppm): 0.99 (bt,  $J$  7.4 Hz, 12H), 1.53-1.66 (m, 8H), 2.35 (bs, 4H), 2.94 (dd,  $J$  4.6, 8.2 Hz, 2H), 3.01 (dd,  $J$  4.9, 8.2 Hz, 2H), 3.21-3.42 (m, 4H), 3.64-3.82 (m, 4H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 50 MHz)  $\delta$  (ppm): 10.1, 29.4, 38.0, 38.3, 72.1, 72.2. MS (ESI, negative):  $m/z$  = 303  $[\text{M-H}]^-$ .

**2,2'-diselanediyl-bis(cyclohexan-1-ol) (3f).**<sup>37</sup> Yellow oil, yield 52% (PE/EtOAc 3:1,  $R_f$  = 0.7; mixture of diastereoisomers).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 200 MHz)  $\delta$  (ppm): 1.22-1.73 (m, 24H), 1.94-2.56 (m, 8H), 2.58-2.75 (m, 2H), 2.80-2.92 (m, 4H), 3.38-3.56 (m, 4H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 50 MHz),  $\delta$  (ppm): 24.5, 26.7, 27.0, 33.2, 34.6, 34.9, 52.0, 52.4, 73.6, 74.1.

**3,3'-diselanediyl-bis(1-N-phthalimidepropan-2-ol) (3h).** Yellow solid, yield 24% (PE/EtOAc 1:1; mixture of diastereoisomers).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 200 MHz)  $\delta$  (ppm): 2.98-3.22 (m, 12H), 3.89-3.95 (m, 8H), 4.18-4.32 (m, 4H), 7.78-7.92 (m, 16H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 50 MHz),  $\delta$  (ppm): 38.7, 42.5, 65.6, 124.3, 124.7, 131.8, 132.5, 132.7, 133.1, 171.2, 171.5. MS (ESI, negative):  $m/z$  = 565  $[\text{M-H}]^-$ .

**N,N'-[(2R,2'R)-diselanediylbis(propane-1,2-diyl)]bis(4-methylbenzenesulfonamide) [(2R,2'R)-6]**<sup>38</sup> Pale yellow solid, yield 55% (PE/EtOAc 3:1,  $R_f$  = 0.5; mixture of diastereoisomers).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm): 1.12 (d,  $J$  6.6 Hz, 6H), 2.42 (s, 6H), 2.94 (dd,  $J$  6.4, 12.8 Hz, 2H), 3.11 (dd,  $J$  5.4, 12.7 Hz, 2H), 3.45-3.68 (m, 2H), 5.15 (d,  $J$  7.4 Hz, 2H), 7.30 (ap d,  $ls$  = 8.2 Hz, 4H), 7.78 (ap d,  $ls$  = 8.2 Hz, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 20.8, 21.5, 37.8, 50.2, 127.1, 129.7, 137.7, 143.4.

## Acknowledgements

We thank MIUR-Italy (Progetto Dipartimenti di Eccellenza 2018–2022 allocated to Department of Chemistry “Ugo Schiff” - DICUS).

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