One-Pot Synthesis of β-Amino/β-Hydroxy Selenides and Sulfides from Aziridines and Epoxides

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Abstract: Diaryl disulfides and diselenides undergo facile cleavage on treatment with rongalite (sodium hydroxymethanesulfinate) to generate the corresponding thiolate and selenolate species in situ, which effect the ring opening of aziridines and epoxides in a regioselective manner. A simple, mild, cost-effective protocol has been developed to prepare β-amino and β-hydroxy sulfides and selenides in a one-pot operation.

Key words: β-amino selenide, β-amino sulfide, β-hydroxy selenide, β-hydroxy sulfide, rongalite, aziridine, epoxide

In recent years the synthesis of peptidomimetic molecules has become an increasingly popular area in the field of drug design.1 Specifically, synthetic routes to sulfanyl- and selanyl-substituted unnatural amino acids and its derivatives, which are the building blocks for the synthesis of modified thio- and seleno-proteins,2 have attracted attention due to their interesting structural and biological properties. The seleno-proteins play an important role in metabolic processes, glutathione peroxidase (GPx) for example, acts as a peroxide scavenger.3a In addition to the interesting properties of thio- and seleno-proteins, simple organosulfur and organoselenium compounds exhibit many useful biological and medicinal properties.4 They are generally targeted as compounds with antioxidant, antitumor, and antimicrobial activity and many of these compounds are competitive inhibitors for target proteins.3b Apart from the biological applications, enantiomerically pure β-amino or β-hydroxy sulfides and selenides are excellent ligands for transition-metal-based asymmetric catalysis.4 Keeping in mind the wide range of applications of these analogues, general synthetic methodologies to prepare sulfur- and selenium-containing derivatives of amino acids in a simple, efficient, stereoregulated manner is greatly appreciated and remains a challenge. A myriad of work has been devoted towards the synthesis of these analogues.5

Unsymmetrical sulfides are generally prepared from alkyl halides by nucleophilic substitution of thiols in the presence of a base and a suitable solvent.7 A number of transition-metal-catalyzed coupling reactions have been developed to synthesize these sulfides, which are shown to be mild and selective.8 Introduction of the selenium moiety is generally carried out by reductive cleavage of diselenides or from selenocyanates followed by coupling with an alkyl halide in one pot, since most of the selenols are unstable and are oxidized spontaneously to the corresponding diselenides in air. Reducing agents, such as NaBH₄, NaN₃, Bu₃SnH, and LiAlH₄, have been used for the synthesis of selenides.9 Ranu et al. developed an indium(I) iodolate mediated cleavage of diaryl diselenides and diaryl disulfides.10

Generally, β-amino or β-hydroxy sulfides and selenides are prepared using the same methodology starting from an amino alcohol, followed by conversion of the hydroxy group into a good leaving group and subsequent nucleophilic substitution with thiolate or in situ generated selenolate.11 Later, aziridines and epoxides were found to be the best starting materials to prepare these analogues in a stereo- and regiocontrolled manner.12 Wakselman et al. demonstrated the synthesis of perfluoroalkyl sulfides by the treatment of perfluoroalkyl halides with an organic disulfide mediated by rongalite.13 Tang et al. reported the synthesis of alkyl aryl sulfides mediated by sodium dithionate, sodium thiosulfate, or rongalite (sodium hydroxymethanesulfinate).1 and compared the rates and percentage of conversion and it was found that rongalite is the most efficient reducing agent for disulfides and for the synthesis of sulfides.14

Following these literature reports, we attempted the synthesis of β-amino and β-hydroxy chalcogenides in a one-pot process mediated by rongalite. Herein, we report our comprehensive study on the aziridine/epoxide ring opening with sulfur and selenium nucleophiles derived from disulfides/diselenides in the presence of rongalite (sodium hydroxymethanesulfinate, 1), which led to an efficient synthesis of β-amino- and β-hydroxy selenides and sulfides from the corresponding diselenides and disulfides under mild conditions (Scheme 1).

Reaction of enantiopure N-tosylaziridine 2 with diphenyl diselenide (3a) mediated by rongalite (1) was carried out by the addition of 3a (0.5 equiv) to a well-stirred solution of aziridine 2 in N,N-dimethylformamide, followed by the addition of potassium carbonate (2 equiv) and rongalite (1, 3 equiv) at room temperature (20 min) resulting in the regioselective ring opening of the aziridine 2 to form the expected β-amino selenide 4a in 98% yield15 (Scheme 2). A mechanism has been proposed for the reduction of diselenide 3a followed by the ring opening of aziridine 2 (Scheme 3).14b Rongalite when treated with a base decomposes to formaldehyde and HSO₃⁻, which transfers a sin-
gle electron to the diselenide resulting in the formation of a radical anion intermediate. The intermediate may spontaneously disproportionate into a radical X and anionic species Y. The selenium radical X further gets reduced to anionic species Y, by another single electron transfer (SET). The attack of Y on aziridine in a regioselective manner at the less hindered carbon gives the desired β-amino selenide.

The mildness of the reaction conditions and the excellent yield obtained encouraged us to explore the scope and generality of the methodology. A wide range of diselenides 3b–g were selected to study the ring-opening reaction with phenylalanine-derived aziridine 2. All diaryl diselenides were synthesized from the corresponding anilines by a diazotization, selenocyanation, and reduction sequence. The results of our study are summarized in Table 1. Diselenides 3b–f reacted with aziridine 2 leading to the corresponding β-amino selenides 4b–f, respectively, in excellent yield. In the case of 2-(4,5-dihydrooxazol-2-yl)-substituted diselenide 3d the cleavage was slower relative to the other diselenides due to steric crowding at the ortho-position. The 4,5-dihydrooxazol-2-yl group is a masked carboxylic acid and it can be deprotected after the reaction.

To expand the scope of this methodology, we decided to study the reactivity of other aziridines bearing different functionalities and complexity in the structure, with diphenyl diselenide 3a. The reaction of aziridines 5a–j with diphenyl diselenide 3a mediated by rongalite (r.t., 20 min), resulted in the formation of the corresponding β-amino selenides 6a–j in excellent yield (Table 2).
Table 1  Synthesis of Phenylalanine-Derived β-Amino Selenides 4

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reactant</th>
<th>R-Se-Se-R</th>
<th>Product</th>
<th>Time</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3a</td>
<td>4a</td>
<td>20 min</td>
<td>98</td>
</tr>
<tr>
<td>2</td>
<td>2 2</td>
<td>3b</td>
<td>4b</td>
<td>30 min</td>
<td>97</td>
</tr>
<tr>
<td>3</td>
<td>2 2 2</td>
<td>3c 4c</td>
<td>4c</td>
<td>30 min</td>
<td>93</td>
</tr>
<tr>
<td>4</td>
<td>2 2 2</td>
<td>3d 4d</td>
<td>4d</td>
<td>60 min</td>
<td>89</td>
</tr>
<tr>
<td>5</td>
<td>2 2 2</td>
<td>3e 4e</td>
<td>4e</td>
<td>20 min</td>
<td>95</td>
</tr>
<tr>
<td>6</td>
<td>2 2 2</td>
<td>3f 4f</td>
<td>4f</td>
<td>20 min</td>
<td>94</td>
</tr>
<tr>
<td>7</td>
<td>2 2 2</td>
<td>3g 4g</td>
<td>no reaction</td>
<td>24 h</td>
<td>–</td>
</tr>
</tbody>
</table>

Table 2  Synthesis of β-Amino Selenides 6 from Diphenyl Diselenide (3a) and Various Aziridines

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reactant</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5a 5a</td>
<td>6a 6a'</td>
<td>20</td>
<td>96</td>
</tr>
<tr>
<td>2</td>
<td>5b 5b</td>
<td>6b</td>
<td>30</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>5c 5c</td>
<td>6c</td>
<td>40</td>
<td>95</td>
</tr>
</tbody>
</table>
Styrene-derived aziridine 5a reacted with diphenyl diselenide (3a) to give an inseparable mixture of regioisomers 6a and 6a¢ in the ratio 1.1:1.19. The regioisomers arise due to similar reactivity profile of the less hindered carbon and the benzylic center. The aziridines 5b–i underwent facile ring opening in the usual manner at the less hindered carbon center to give the desired products 6b–h. In the case of the trisubstituted aziridine 5f, the reaction gave a 1.7:1 regioisomeric mixture of products 6f/6f¢. This can be explained on the basis of the competition of nucleophilic attack in a SN1 like pathway at the tertiary center and SN2 fashion at the secondary center. The same kind of regioisomeric mixture 6i/6i¢ is obtained in the methylcyclohexene-derived aziridine 5i. Since deprotection of the tosyl group involves harsh conditions, the same methodology has been demonstrated using benzylxycarbonyl (Cbz) protected aziridine 5j. The Cbz-protected aziridine 5j underwent ring opening smoothly in 45 minutes to give the β-amino selenide 6j in 95% yield.

When propylene oxide was treated with diphenyl diselenide (3a) and rongalite, the reaction proceeded cleanly (DMF, r.t., 20 min) to give the β-hydroxy selenide 8a in 87% yield (Scheme 4).

**Scheme 4** Nucleophilic ring opening of epoxides with diphenyl diselenide (3a) mediated by 1.

The scope of the methodology was further investigated by using various epoxides to study the reactivity. The epoxides 7b–h were treated with diphenyl diselenide (3a) and rongalite under the same conditions leading to the formation of β-hydroxy selenides 8b–h in excellent yields (Table 3). Ring opening in the case of styrene oxide (7b),
(unlike the styrene-derived aziridine 5a) resulted in a single regioisomer 8b in 95% yield following the SN2 pathway exclusively. The reaction was further extended to bis-epoxides, to give bis-selenides. The reaction of bis-epoxide 7g yielded the corresponding bis-selenide 8g (93%). The bis-selenide 8g is an important precursor for making the trans-furofuran moiety in the total synthesis of (−)-ku-mausallene.20 Similarly, in the reaction of epibromohyrdrin 7h, the corresponding bis-selenide 8h was obtained in 92% yield.

Having demonstrated the ability of rongalite to cleave the diselenide bond and its application to the synthesis of β-amino selenides and β-hydroxy selenides, the chemistry was extended to the synthesis of β-amino sulfides and β-hydroxy sulfides by reductive cleavage of diaryl disulfides.

As in the case of diselenides, disulfides can also undergo reductive cleavage in the presence of rongalite. The reaction was carried out by the addition of diphenyl disulfide (9a, 0.5 equiv) to a solution of phenylalanine-derived aziridine 2 in N,N-dimethylformamide, followed by the addition of potassium carbonate (2 equiv). The mixture was stirred vigorously followed by the addition of rongalite (3 equiv).15 The reaction proceeded smoothly (20 min) to give the corresponding β-amino sulfide 10a as the sole product in 96% yield (Scheme 5). The facile reactivity and the excellent yield obtained encouraged us to explore the reaction with various disulfides to check the generality of this methodology.

Phenylalanine-derived aziridine 2 was taken as a standard and reacted with various organic disulfides. The reaction of disulfides 9b–f with aziridine 2 mediated by rongalite

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**Table 3** Synthesis of β-Hydroxy Selenides 8 from Diphenyl Diselenide (3a) and Various Epoxides

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reactant</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7b</td>
<td>8b</td>
<td>20</td>
<td>97</td>
</tr>
<tr>
<td>2</td>
<td>7c</td>
<td>8c</td>
<td>20</td>
<td>95</td>
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<tr>
<td>3</td>
<td>7d</td>
<td>8d</td>
<td>20</td>
<td>91</td>
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</tr>
<tr>
<td>7</td>
<td>7h</td>
<td>8h</td>
<td>30</td>
<td>92</td>
</tr>
</tbody>
</table>

*a All compounds except 7d were racemic, p-NO2Bz = p-nitrobenzoyl.

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**Scheme 5** Nucleophilic ring opening of 2 with diphenyl disulfide (9a) mediated by 1

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gave the corresponding β-amino sulfides 10b–e in excellent yield (Table 4). As in the case of dibenzyl diselenide (3g), dibenzyl disulfide (9f) also failed to react with aziridine 2 even after 24 hours.

The methodology was further extended to various aziridines. The aziridines 5a–k were treated with diphenyl disulfide (9a, 0.5 equiv) followed by the addition of potassium carbonate and rongalite and the reaction (r.t., 20 min) resulted in the formation of β-amino sulfides 11a–k in excellent yields (Table 5). In the case of styrene-derived aziridine 5a, the reaction led to a regioisomeric mixture of β-amino sulfides 11a/11a’ in 1:1 ratio with a total yield of 96%.

The aziridines 5d,e underwent ring opening smoothly from the less hindered side. Since the isopropyl group blocks the approach of the incoming nucleophile, the nucleophile attacks at the less hindered side of the aziridine to give 10d,e as the sole products in excellent yield. With trisubstituted aziridine 5f, a regioisomeric mixture of β-amino sulfides 11f and 11f’ were formed in 90% yield in the ratio 3:1. Cbz-protected aziridine 5j was successfully converted into Cbz-β-amino sulfide 11j in 96% yield, which can be converted into the free amine by simple deprotection.

Following the efficient ring opening of aziridines, the reaction was extended to study the ring opening of epoxides. To compare the reactivity differences between the selenium and sulfur nucleophiles, the same set of epoxides were taken for the study. Initially, propylene oxide 7a was treated with diphenyl disulfide (9a) and rongalite in N,N-dimethylformamide to give 12a as the sole product in 93% yield (Scheme 6). The reaction of various epoxides 7b–h with diphenyl disulfide (9a) and rongalite gave the corresponding β-hydroxy sulfides 12b–h in excellent yields (Table 6).

### Table 4  Synthesis of Phenylalanine-Derived β-Amino Sulfides 10

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reactant</th>
<th>R-S-S-R</th>
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<th>Time</th>
<th>Yield (%)</th>
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<tbody>
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<td>1</td>
<td>2 Ph</td>
<td>9a</td>
<td>10a</td>
<td>20 min</td>
<td>96</td>
</tr>
<tr>
<td>2</td>
<td>2 Me</td>
<td>9b</td>
<td>10b</td>
<td>30 min</td>
<td>96</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>9c</td>
<td>10c</td>
<td>30 min</td>
<td>92</td>
</tr>
<tr>
<td>4</td>
<td>2 Cl</td>
<td>9d</td>
<td>10d</td>
<td>20 min</td>
<td>94</td>
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<tr>
<td>5</td>
<td>2 O2N</td>
<td>9e</td>
<td>10e</td>
<td>20 min</td>
<td>95</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>9f</td>
<td>no reaction</td>
<td>24 h</td>
<td>–</td>
</tr>
</tbody>
</table>

gioselective manner under mild conditions in a one-pot operation. The methodology would be of interest due to the cost-effective and metal-free reaction conditions and high yield. The reaction has been extended further to the ring opening of epoxides in a stereospecific and regiose-

Table 5: Synthesis of β-Amino Sulfides 11 from Diphenyl Disulfide (9a) and Various Aziridines

<table>
<thead>
<tr>
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<th>Product</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5a</td>
<td>11a, 11a’</td>
<td>20</td>
<td>96 (1:1)b</td>
</tr>
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<td>5b</td>
<td>11b</td>
<td>30</td>
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</tr>
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<td>3</td>
<td>5c</td>
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<td>95</td>
</tr>
<tr>
<td>4</td>
<td>5d</td>
<td>11d</td>
<td>40</td>
<td>94</td>
</tr>
<tr>
<td>5</td>
<td>5e</td>
<td>11e</td>
<td>40</td>
<td>92</td>
</tr>
<tr>
<td>6</td>
<td>5f</td>
<td>11f, 11f’</td>
<td>30</td>
<td>90 (3:1)b</td>
</tr>
<tr>
<td>7</td>
<td>5g</td>
<td>11g</td>
<td>30</td>
<td>92</td>
</tr>
<tr>
<td>8</td>
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<td>11h</td>
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<td>93</td>
</tr>
<tr>
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<td>5i</td>
<td>11i, 11i’</td>
<td>30</td>
<td>89 (4:1)b</td>
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<tr>
<td>10</td>
<td>5j</td>
<td>11j</td>
<td>45</td>
<td>96</td>
</tr>
<tr>
<td>11</td>
<td>5k</td>
<td>11k</td>
<td>30</td>
<td>94</td>
</tr>
</tbody>
</table>

a Compounds 5a–i, 5k are racemic and the relative stereochemistry is represented. 5j was derived enantiomerically pure from L-phenylalanine.
b Based on the 1H NMR integration values.
Table 6 Synthesis of β-Hydroxy Sulfides 12 from Diphenyl Disulfide (9a) and Various Epoxides

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reactanta</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7b</td>
<td>12b</td>
<td>20</td>
<td>97</td>
</tr>
<tr>
<td>2</td>
<td>7c</td>
<td>12c</td>
<td>20</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>p-NO2BzO</td>
<td>12d</td>
<td>20</td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>7e</td>
<td>12e</td>
<td>20</td>
<td>93</td>
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<td>5</td>
<td>7f</td>
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</tr>
<tr>
<td>7</td>
<td>7h</td>
<td>12h</td>
<td>30</td>
<td>94</td>
</tr>
</tbody>
</table>

a All compounds except 7d were racemic; p-NO2Bz = p-nitrobenzoyl.

Selective manner for the synthesis of β-hydroxy sulfides and selenides in excellent yields.

All reactions were carried out in oven-dried apparatus using dry solvents under anhydrous conditions, unless otherwise noted. Reaction mixtures were stirred magnetically unless otherwise stated. Commercial grade solvents were distilled and dried according to literature procedures.21 Analytical TLC was performed on commercial plates coated with silica gel GF 254 (0.25 mm). Silica gel (230–400 mesh) was used for column chromatography. Melting points determined are uncorrected. Yields refer to chromatographically and spectroscopically (H NMR) homogeneous materials, unless otherwise stated. IR spectra were recorded on a FT-IR spectrometer.

NMR spectra were recorded on 300 or 400 MHz instruments and chemical shifts are cited with respect to SiMe4 as internal (H and 13C) and MeSe (77Se) as external standard. High resolution mass spectra (HR-MS) were recorded on an electro-spray mass spectrometer. All novel compounds were fully characterized. All known compounds had spectroscopic data consistent with the literature: 4a,21a 6a,21b 6b,22a 6h,22b 8a,21c 10b,22a 10d,22b 11a,22c 11c,22c 11g,22c 11h,22c 11j,22c 11k,22c 12a,22b 12b,22b 12f,22d 12h,22a 11c,22c r.t. = 28 °C.

β-Amino Selenides or β-Hydroxy Selenides; General Procedure

To a well-stirred soln of aziridine or epoxide (0.2 mmol, 1 equiv) in DMF (2 mL) was added the diselenide (0.1 mmol, 0.5 equiv) followed by K2CO3 (0.4 mmol, 2 equiv) and rongalite (1.0 mmol, 3 equiv). The mixture was stirred at r.t. for 30–60 min (TLC monitoring). After complete consumption of the starting material, H2O was added to quench the reaction and it was extracted with CH2Cl2 (2 × 10 mL). The organic layer was separated and dried (anhyd Na2SO4). The crude product was purified by column chromatography (silica gel).

(5)-1-Phenyl-3-(4-tolylselenyl)-N-tosylpropan-2-amine (4b)

Colorless oil; yield: 97%; Rf = 0.3 (EtOAc–hexanes, 2:8).

[a]D25 = –2.9 (c 2, CHCl3).


(5)-1-(1-Naphthylselenyl)-3-phenyl-N-tosylpropan-2-amine (4d)

Colorless oil; yield: 93%; Rf = 0.4 (EtOAc–hexanes, 2:8).

[a]D25 = –67.3 (c 1, CHCl3).

IR (neat): 3276, 3054, 2923, 1498, 1328, 1158, 748, 665 cm–1.

1H NMR (300 MHz, CDCl3): δ = 8.27–7.84 (m, 1 H), 7.88–7.81 (m, 2 H), 7.69 (d, J = 6.0 Hz, 1 H), 7.57–7.52 (m, 2 H), 7.37 (t, J = 39.0 Hz, 1 H), 7.34 (m, 2 H), 7.16–7.11 (m, 3 H), 6.88 (d, J = 5.4 Hz, 4 H), 4.76 (d, J = 7.2 Hz, 1 H), 3.53–3.42 (m, 2 H), 3.10 (dd, J = 4.5, 12.9 Hz, 1 H), 2.99 (dd, J = 6.6, 13.8 Hz, 1 H), 2.83–2.76 (m, 2 H), 2.26 (s, 3 H).

13C NMR (75 MHz, CDCl3): δ = 142.9, 136.6, 136.5, 134.1, 132.8, 129.5, 129.3, 129.2, 128.7, 128.6, 128.4, 127.4, 126.8, 126.7, 126.6, 126.3, 125.8, 54.5, 40.3, 32.7, 31.4.

77Se NMR (75 MHz, CDCl3): δ = 236.096.


(5)-1-[2-(5,5-Dimethyl-4,5-dihydrooxazol-2-yl)phenylselenyl]-3-phenyl-N-tosylpropan-2-amine (4d)

Colorless oil; yield: 89%; Rf = 0.3 (EtOAc–hexanes, 3:7).

[a]D25 = –34.1 (c 1, CHCl3).

IR (neat): 3281, 2968, 2960, 1646, 1455, 1314, 1157, 1030, 963, 813, 733, 655 cm–1.

1H NMR (300 MHz, CDCl3): δ = 7.70 (m, 1 H), 7.45 (d, J = 6.0 Hz, 2 H), 7.26–7.19 (m, 6 H), 7.05–7.00 (m, 4 H), 5.74 (d, J = 5.4 Hz, 1 H), 4.10 (s, 2 H), 3.62–3.57 (m, 1 H), 3.02–2.92 (m, 3 H), 2.76 (dd, J = 4.8, 9.9 Hz, 1 H), 2.32 (s, 3 H), 1.45 (s, 3 H), 1.44 (s, 3 H).

13C NMR (75 MHz, CDCl3): δ = 162.1, 143.4, 137.5, 133.1, 131.4, 131.3, 130.4, 129.9, 129.4, 129.1, 127.3, 127.2, 126.2, 79.4, 69.1, 59.6, 41.5, 32.3, 29.1, 29.0, 22.0.

77Se NMR (75 MHz, CDCl3): δ = 255.64.

(S)-1-(4-Chlorophenylselanyl)-3-phenyl-N-tosylpropan-2-amine (4e)
Yield: 95%; mp 62 °C; \( R_f = 0.4 \) (EtOAc–hexanes, 2:8).
\([\alpha]_{D}^{25} = -54.4 \) (c 2, CHCl₃).
IR (neat): 3282, 2924, 1598, 1475, 1325, 1159, 1090, 813, 743, 700, 665 cm⁻¹.

\( ^1H \) NMR (300 MHz, CDCl₃): \( \delta = 7.41 \) (d, \( J = 7.8 \) Hz, 2 H), 7.31 (d, \( J = 8.4 \) Hz, 2 H), 7.22–7.03 (m, 7 H), 6.93–6.90 (m, 2 H), 4.88 (d, \( J = 6.9 \) Hz, 1 H), 3.51–3.36 (m, 1 H), 3.12 (dd, \( J = 4.8, 12.9 \) Hz, 1 H), 2.94 (dd, \( J = 6.3, 13.8 \) Hz, 1 H), 2.87–2.69 (m, 2 H), 2.38 (s, 3 H).

\( ^13C \) NMR (75 MHz, CDCl₃): \( \delta = 143.2, 136.3, 134.1, 129.5, 129.3, 129.1, 128.6, 128.4, 126.9, 126.7, 126.4, 54.4, 40.2, 33.11, 21.5.

\( \text{Se NMR (75 MHz, CDCl₃): } \delta = 245.881. \)
HRMS: \( m/z [M + Na]^+ \) calcd for C₁₉H₁₈NNaO₂Se: 434.0669; found: 434.0676.

(3R*,4S*)-2-Methyl-4-(phenylselanyl)-N-tosylpentan-3-amine (6d)
Colorless oil; yield: 92%; \( R_f = 0.3 \) (EtOAc–hexanes, 1:9).
IR (neat): 3480, 2962, 2939, 2784, 1626, 1600, 1443, 1325, 1164, 1090, 1033, 747, 667 cm⁻¹.

\( ^1H \) NMR (300 MHz, CDCl₃): \( \delta = 7.69 \) (d, \( J = 8.1 \) Hz, 2 H), 7.40–7.37 (m, 2 H), 7.31–7.17 (m, 5 H), 4.94 (d, \( J = 9.9 \) Hz, 1 H), 3.36 (ddd, \( J = 0.1, 0.9, 4.5 \) Hz, 1 H), 3.15–3.06 (m, 1 H), 2.38 (s, 3 H), 2.09–1.99 (m, 1 H), 1.38 (d, \( J = 7.5 \) Hz, 3 H), 0.84 (d, \( J = 5.1 \) Hz, 6 H).

\( ^13C \) NMR (75 MHz, CDCl₃): \( \delta = 143.0, 138.6, 134.4, 129.6, 129.4, 129.0, 127.7, 126.9, 63.0, 45.4, 29.9, 21.5, 21.0, 20.4, 17.3, 16.9.

\( \text{Se NMR (75 MHz, CDCl₃): } \delta = 363.35. \)
HRMS: \( m/z [M + Na]^+ \) calcd for C₁₉H₂₅NNaO₂Se: 434.0669; found: 434.0646.

(3R*,4R*)-2-Methyl-4-(phenylselanyl)-N-tosylhexan-3-amine (6c)
Colorless oil; yield: 95%; mp 74 °C; \( R_f = 0.3 \) (EtOAc–hexanes, 2:8).
IR (neat): 3273, 2978, 2853, 1590, 14, 1356, 1150, 1190, 1030, 823, 746, 665 cm⁻¹.

\( ^1H \) NMR (300 MHz, CDCl₃): \( \delta = 7.66 \) (d, \( J = 7.8 \) Hz, 2 H), 7.38 (d, \( J = 7.8 \) Hz, 2 H), 7.30–7.22 (m, 5 H), 5.13 (d, \( J = 4.2 \) Hz, 1 H), 3.53 (ddd, \( J = 3.0, 4.2, 12.9 \) Hz, 1 H), 3.18–3.11 (m, 1 H), 2.39 (s, 3 H), 1.96–1.80 (m, 1 H), 1.25 (d, \( J = 6.9 \) Hz, 3 H), 0.80 (d, \( J = 7.2 \) Hz, 3 H), 0.75 (d, \( J = 6.6 \) Hz, 3 H).

\( ^13C \) NMR (75 MHz, CDCl₃): \( \delta = 142.9, 138.7, 135.3, 129.4, 129.0, 128.4, 127.8, 126.9, 64.8, 44.0, 31.6, 21.4, 20.6, 20.3, 19.5.

\( \text{Se NMR (75 MHz, CDCl₃): } \delta = 342.3. \)
HRMS: \( m/z [M + Na]^+ \) calcd for C₁₉H₂₅NNaO₂Se: 434.0669; found: 434.0682.
$^{77}$Se NMR (75 MHz, CDCl$_3$): $\delta = 240.56$.
HRMS: $m/z$ [M + Na]$^+$ calcld for C$_{23}$H$_{23}$NNaO$_2$Se: 448.0792; found: 448.08.

(1-Phenylselenyl)hex-5-en-1-ol (8c)

IR (neat): 3417, 3173, 2927, 1428, 1032, 920, 746, 687 cm$^{-1}$.

$^{13}$C NMR (75 MHz, CDCl$_3$):

117.2, 72.7, 69.4, 31.8.

$^{1}H$ NMR (300 MHz, CDCl$_3$):

$J = 7.53–7.50$ (m, 2 H), 7.26–7.21 (m, 2 H), 5.92–5.79 (m, 1 H), 5.28–5.14 (m, 2 H), 3.96–3.88 (m, 3 H), 3.54–3.43 (m, 3 H), 3.12–2.86 (m, 2 H), 2.85 (dd, $J = 4.2$ Hz, 1 H).

C NMR (75 MHz, CDCl$_3$):

$\delta = 164.2$, 134.3, 132.6, 129.6, 129.1, 127.0, 117.2, 72.7, 69.4, 31.8.

HRMS: $m/z$ [M + Na]$^+$ calcld for C$_{17}$H$_{17}$NNaO$_2$Se: 327.0264; found: 327.0264.

$\beta$-Amino Sulfides/$\beta$-Hydroxy Sulfides; General Procedure

To a well-stirred soln of aziridine or epoxide (0.2 mmol, 1 equiv) in DMF (2 mL) was added the disulfide (0.1 mmol, 0.5 equiv) followed by K$_2$CO$_3$ (0.4 mmol, 2 equiv) and rongalite (1, 0.6 mmol, 3 equiv). The mixture was stirred at r.t. for 30–60 min (TLC monitoring). After complete consumption of the starting material, H$_2$O was added to quench the reaction and it was extracted with CH$_2$Cl$_2$ (2×10 mL). The organic layer was separated and dried (anhyd Na$_2$SO$_4$). The crude product was further purified by column chromatography (silica gel).

(5)-1-Phenyl-3-(2-pyridylsulfanyl)-N-tosylpropan-2-amine (10c)

Yield: 92%; mp 76°C; $R_f$ = 0.5 (EtOAc–hexanes, 2:8).

IR (neat): 3417, 3173, 2927, 1428, 1032, 920, 746, 687 cm$^{-1}$.

$^{13}$C NMR (75 MHz, CDCl$_3$):

115.9, 115.8, 114.9, 69.4, 37.0, 35.6, 30.0.

$^{77}$Se NMR (75 MHz, CDCl$_3$): $\delta = 233.71$.

HRMS: $m/z$ [M + Na]$^+$ calcld for C$_{21}$H$_{22}$N$_2$NaO$_2$S$_2$: 421.1020; found: 421.1016.

(4)-[3-(4-Nitrophenylsulfanyl)-1-phenyl-3-(2-pyridylsulfanyl)]-tosylpropan-2-amine (10c)

Yield: 95%; mp 121°C; $R_f$ = 0.4 (EtOAc–hexanes, 3:7).

IR (neat): 3483, 3293, 2966, 3931, 2874, 1635, 1508, 1440, 1325, 1159, 1092, 739, 665 cm$^{-1}$.

$^{1}H$ NMR (300 MHz, CDCl$_3$):

$\delta = 8.11$ (d, $J = 8.1$ Hz, 2 H), 7.48 (d, $J = 8.1$ Hz, 2 H), 7.27–7.18 (m, 5 H), 6.99 (d, $J = 6.3$ Hz, 2 H), 6.98–6.95 (m, 2 H), 4.90 (d, $J = 6.9$ Hz, 1 H), 3.59–3.48 (m, 1 H), 3.30 (dd, $J = 4.5$, 13.8 Hz, 1 H), 3.08–2.93 (m, 2 H), 2.77 (dd, $J = 6.9$, 13.8 Hz, 1 H), 2.37 (s, 3 H).

HRMS: $m/z$ [M + Na]$^+$ calcld for C$_{21}$H$_{22}$N$_2$NaO$_2$S$_2$: 465.0914; found: 465.0914.

(3)-[3-(4-Nitrophenylsulfanyl)-1-phenyl-3-(2-pyridylsulfanyl)]-tosylpropan-2-amine (10c)

Yield: 95%; mp 121°C; $R_f$ = 0.4 (EtOAc–hexanes, 3:7).

IR (neat): 3483, 3293, 2966, 3931, 2874, 1635, 1508, 1440, 1325, 1159, 1092, 739, 665 cm$^{-1}$.

$^{1}H$ NMR (300 MHz, CDCl$_3$):

$\delta = 8.44$–8.42 (m, 1 H), 7.93 (d, $J = 4.2$ Hz, 2 H), 7.56 (d, $J = 8.4$ Hz, 2 H), 7.49 (dt, $J = 2.1$, 7.2 Hz, 1 H), 7.31–7.05 (m, 9 H), 3.61–3.52 (m, 1 H), 4.23 (dd, $J = 4.2$, 13.5 Hz), 3.03 (dd, $J = 7.5$, 14.7 Hz, 1 H), 2.97–2.88 (m, 2 H), 2.36 (s, 3 H).

HRMS: $m/z$ [M + Na]$^+$ calcld for C$_{21}$H$_{22}$N$_2$NaO$_2$S$_2$: 465.0914; found: 465.0914.
H NMR (300 MHz, CDCl₃): δ = 7.72 (d, J = 8.4 Hz, 2 H), 7.26–7.19 (m, 7 H), 4.97 (d, J = 9.9 Hz, 1 H), 3.41–3.34 (m, 1 H), 3.14–3.06 (m, 1 H), 2.39 (s, 3 H), 2.11–1.99 (m, 1 H), 1.23 (d, J = 6.9 Hz, 3 H), 0.88–0.84 (m, 6 H).

13C NMR (75 MHz, CDCl₃): δ = 135.5, 134.2, 129.5, 128.9, 126.2, 117.2, 72.3, 72.2, 68.9, 37.3.


(2R,3R,4R)-1,4-Bis(phenylsulfanyl)butane-2,3-diol (12g)

Colorless oil; yield: 94%; Rf = 0.5 (EtOAc–hexanes, 4:6).

IR (neat): 3483, 3293, 2966, 3931, 2874, 1635, 1598, 1440, 1325, 1159, 1093, 1033, 747, 667 cm⁻¹.

1H NMR (300 MHz, CDCl₃): δ = 7.34–7.16 (m, 5 H), 3.73 (dd, J = 5.4, 8.7 Hz, 1 H), 3.12–3.07 (m, 2 H), 3.91 (d, J = 5.4 Hz, 1 H).

13C NMR (75 MHz, CDCl₃): δ = 134.8, 129.9, 120.0, 126.6, 70.2, 38.1.


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References


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(15) After the addition of rongalite, the mixture turned orange yellow in the case of diselenides, due to the formation of selenolate ion and yellow in the case of disulfides, due to formation of the thiolate. The color disappeared at the completion of the reaction.


(18) All the aziridines were generally prepared from the corresponding alkenes: Jeong, J. U.; Tao, B.; Sagasser, L.; Henniges, H.; Sharpless, K. B. *J. Am. Chem. Soc.* 1998, 120, 6844.

(19) The ratio of regioisomers was determined based on the integration values of 1H NMR.


