Diastereoselective Synthesis of 2-Phenylselenenyl-1,3-anti-Diols and 2-Phenylselenenyl-1,3-anti-Azido-Alcohols via Hydroxy- and Azido-Selenenylation Reactions

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Abstract: A method to synthesize 2-phenylselenenyl-1,3-anti-diols and 2-phenylselenenyl-1,3-anti-azidoalcohols via hydroxy- or azido-selenenylation of trans-allylic alcohols is reported. Moreover, the first example of hydroxyl-selenenylation of an allylic azide is presented. Yields ranging from moderate to good and diastereomeric ratios up to 95:5 are achieved.

Keywords: Azides, diols, seleniranium ion.

Introduction

The 1,3-diol system is frequently found in the structure of biologically active natural products such as the macrolide antibiotics [1], and consequently, a wide variety of synthetic methods have been developed for these targets [2]. Moreover, chiral 1,3-aminoalcohol sequences are found in compounds of biological interest such as nucleoside antibiotics or in alkaloids. Indeed, several synthetic approaches to these moieties have been developed [3].

In the last years our group has been involved in the stereoselective synthesis of substituted oxygenated heterocyclic rings, such as tetrahydrofurans, tetrahydropryans, δ- and γ-lactones, using electrophilic organoselenium reagents [4]. Mild reaction conditions and easy removal or subsequent functionalization of the phenylselenenyl residue are the major advantages of this chemistry [5].

Here we report a simple approach for the synthesis of open chain molecules such as 2-phenylselenenyl-1,3-diols and 2-phenylselenenyl-1,3-azido-alcohols, as precursors of 1,3-diols and...
1,3-aminoalcohols. Recently we reported two examples of direct hydroxyl-selenenylation reactions of trans-allylic alcohols with good diastereoselectivity [4a]. This reaction has not been studied in detail [6]. We then exploited this reaction with other compounds together with the electrophilic azido-selenenylation reaction [7]. It has been reported that the addition of PhSeN$_3$ to simple alkenes, as well as to activated alkenes, proceeds stereospecifically but not regiospecifically [8]. A radical process for azido-phenylselenenylation of double bonds has been also reported [9]. Recently, 2-phenylselenenyl-1,3-syn-diols have been prepared by a cross-aldol reaction between benzaldehyde and β-phenylselenenylenoxysilanes followed by borane reduction [10]. Some 2-phenylselenenyl-1,3-syn-diols have been obtained by electrophilic addition of benzeneselenenic acid to allylic alcohols [11].

**Results and Discussion**

Compounds 1a-g were used as starting materials for our study.

|   | R$^1$ | R$^2$ |   | R$^1$ | R$^2$ |
|---|-------|-------|---|-------|-------|
| a | Me    | Ph    | e | Ph    | Ph    |
| b | i-Pr  | Ph    | f | EtOCOCH$_2$ | Ph    |
| c | Me    | p-Cl-Ph | g | Me    | CH$_2$Ph |
| d | Me    | Me    |

**Scheme 1**

First we studied the electrophilic hydroxy-selenenylation of alcohols 1a-f. We used for this purpose phenylselenenyl chloride in acetonitrile/water at room temperature. The intermediate seleniranium ion formed is attacked by the nucleophile, a water molecule, to give the diols 2 and 3. Yields ranged from moderate to good, with the less reactive compound being the alkyl substituted allylic alcohol 1d, whereas diastereomeric ratios were good, being at least 90:10. With R$^1$ groups bigger than methyl, slight improvement in the ratios was observed.

**Scheme 2**
Table 1. Hydroxy-selenenylation of compounds 1a-f.

| Entry | Compd. 2+3 (%) | 1 (%) | 2:3 |
|-------|----------------|-------|-----|
| 1     | 1a             | 88    | 11  | 90:10 |
| 2     | 1b             | 69    | 32  | 95:5  |
| 3     | 1c             | 63    | 24  | 92:8  |
| 4     | 1d             | 55    | 40  | 91:9  |
| 5     | 1e             | 77    | 11  | 94:6  |
| 6[a]  | 1f             | 80    | <5% | 95:5  |

The stereochemistry of the major diastereoisomer was verified by the 1H-NMR spectra of compounds 2d-e and 3d-e. Indeed, the CHSePh signal in the major diastereoisomers 2d-e was a dd, while in the minor diastereoisomers 3d-e it was a triplet because of their symmetry. The stereochemical outcome of the reaction is depicted in the Scheme 2. Seleniranium ions 6 and 7 arise from the attack of the electrophilic PhSeCl on both sides of the carbon-carbon double bond. As a consequence of the stabilizing Se—O interaction, seleniranium ion 7 is less stable because of the steric interaction between the R^1 group and hydrogen atom. In seleniranium ion 6 this interaction is absent.

Then we studied the electrophilic azido-selenenylation of alcohols 1. Preliminary investigations were carried out on compound 1a in order to find the best conditions. We considered different amounts of sodium azide, solvents and sources of electrophilic selenium reagent. Reactions were carried out for 24 h at room temperature. Results are reported in Table 2. Significant yield improvements were obtained using five equiv. of NaN₃ instead of three equiv., however a further increase of the amount of NaN₃ did not give improved yields but rather a less clean reaction (Table 2, entries 1-3). The use of other solvents such as dimethylformamide, acetonitrile and dimethoxyethane in place of dimethylsulfoxide gave poor yields (Table 2, entries 2,4-6). The use of the more reactive phenylselenenyl triflate gave better yields both in acetonitrile and dimethylsulfoxide, being, indeed, the latter the best conditions found (entries 7,8).

Table 2. Azido selenenylation of compound 1a.

| Entry | PhSeX | Solvent | 4+5 (%) | 1 (%) | 4/5 |
|-------|-------|---------|---------|-------|-----|
| 1⁴    | PhSeCl| DMSO    | 50      | 8     | 86/14 |
| 2     | PhSeCl| DMSO    | 66      | 7     | 84/16 |
| 3     | PhSeCl| DMSO    | 46      | 18    | 85/15 |
| 4     | PhSeCl| DMF     | 20      | 45    | 81/19 |
| 5     | PhSeCl| MeCN    | 32      | 40    | 88/12 |
| 6     | PhSeCl| DME     | 1       | 99    | -    |
| 7     | PhSeOTf| MeCN   | 43      | 29    | 87/13 |
| 8     | PhSeOTf| DMSO    | 73      | 10    | 87/13 |
| 9     | PhSeCl| bmimBF₄| 24      | 20    | 81/19 |

⁴ NaN₃ 10 eq.; ⁵ NaN₃ 5 eq.; ⁶ NaN₃ 3 eq.
In each case the diastereoselectivity found is very similar (87:13, as determined by $^1$H-NMR). Finally, the reaction was carried out in the ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate (bmimBF$_4$). The yield was poor and no improvement in diastereoselectivity was observed. Moreover, a 20% yield of compounds 2a and 3a was obtained with high ratio (94:6) [12].

In order to establish the stereochemistry of the major product, the mixture of 4a and 5a was separated by column chromatography. The major product was reduced with triphenylphosphine and then treated with 1,1'-carbonyldiimidazole to give the cyclic urethane 9 (Scheme 3). The $^1$H-NMR spectrum showed that the coupling constants are small (see Experimental) confirming in this manner the structure proposed.

![Scheme 3](image)

$i$: PPh$_3$, THF/H$_2$O, r.t.; $ii$: 1,1'-carbonyldiimidazole, CH$_2$Cl$_2$.

Using our best conditions (PhSeOTf 1eq., DMSO, NaN$_3$ 5 eq.), we carried out the azido-selenenylation on compounds 1b-g (Table 3). Yields were not high and, usually, a considerable amount of starting material was recovered (30-45%). No significant change in diastereoselectivity was found, being lower in the case of 1f; however, for substrates possessing an alkyl group as substituent on the C=C double bond (1d,g), somewhat higher selectivities were observed. Protection of the hydroxy group in 1a as benzyl or TBDMS ether gave poor yields in the azido-selenenylation [13].

| Entry | Compd. | 4+5  | 1  | 4/5  |
|-------|--------|------|----|------|
| 1     | 1a     | 73   | 10 | 87:13|
| 2     | 1b     | 51   | 45 | 84:16|
| 3     | 1c     | 64   | 30 | 83:17|
| 4     | 1d     | 58   | 40 | 92:8 |
| 5     | 1e     | 33   | 33 | 87:13|
| 6     | 1f     | 48   | 43 | 82:18|
| 7     | 1g     | 57   | 35 | 93:7 |

In order to prepare 2-phenylselenenyl-1,3-azido alcohols a different approach can be followed. We reasoned that using an allylic azide as starting material and water as nucleophile better yields could be reached. However, this approach suffers a limitation: allylic azides exist as an equilibrating mixture of regioisomers [14]. Such rearrangement can be suppressed in compounds in which the allylic azide is conjugated. To explore this notion we used compound 10 (Scheme 4).
Under the usual conditions we obtained compounds 11 and 12 in 74% yield and 90:10 ratio. Quenching the reaction after one hour we observed a lower yield (63%); moreover, an even lower yield (55%) was also obtained if water is added to a solution containing compound 10 and PhSeCl in CH$_3$CN. In each case the 11:12 ratio did not change. It is noteworthy that the 11:12 ratio is identical to the 2a:3a ratio, leading us to conclude that both the OH and N$_3$ groups play a similar role.

Finally, we used compound 4a for further transformation. It is known that hydroxyselenides can be transformed into epoxides [15]. Treatment of 4a with 1.2 equiv. of $m$-chloroperbenzoic acid/K$_2$CO$_3$ in methanol at -10 °C did not afford the expected product. Rather, oxidative elimination via selenoxide syn-elimination took place to give compound 13 in 65% yield. However, when the reaction was carried out with 5 equiv. the cis-epoxide 14 [16] was obtained in 40% yield. In the presence of an excess of MCPBA the reactive intermediate is the selenone. It would appear that because of the excellent leaving-group properties of the PhSeO$_2$ group, the reaction indeed took place, but, probably due to steric hindrance, the yield was not high. The cis-stereochemistry was established by $^1$H-NMR ($J_{H2H3} = 4.2$ Hz). Although the yield was not high this methodology allows the stereoselective synthesis of 1-azido-2,3-cis-epoxides, useful compounds for further manipulations.

Conclusions

We have presented a facile route for the synthesis of 2-phenylselenenyl-1,3-anti-diols and 2-phenylselenenyl-1,3-anti-azido-alcohols with interesting diastereoselectivities and complete regioselectivity.

Acknowledgments

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Experimental

General

$^1$H-NMR and $^{13}$C NMR spectra were recorded on a Bruker AC-E series 250 MHz spectrometer as CDCl$_3$. When a minor diastereoisomer was obtained in pure form, spectra and analytical data are reported. When minor diastereoisomers were obtained as mixtures, the distinguishable signals are reported. IR spectra were recorded on a Shimadzu model FTIR 8300 infrared spectrophotometer using NaCl cells. Flash chromatography was carried out using Macherey-Nagel silica gel (0.04-0.063 mm). Light petroleum refers to the fraction boiling in the range 40-60 °C. Compounds 1a and 1e were prepared by sodium borohydride reduction of the corresponding commercially available ketones; compound 1b by reaction of cinnamaldehyde with i-propylmagnesium chloride; compounds 1c and 1g by sodium borohydride reduction of the corresponding ketone obtained by Wittig reaction; compound 1d by reaction of trans-crotonaldehyde with methylmagnesium chloride; compound 1f by reaction of cinnamaldehyde with lithium enolate of ethyl acetate and compound 8 by reaction with NaN$_3$ on the acetyl derivative of compound 1a in the presence of Pd(PPh$_3$)$_4$ [17]. All compounds showed spectroscopic and analytical data in agreement with their structures.

General procedure for hydroxy-selenenylation reactions:

To a stirred solution of compounds 1a-f in acetonitrile (2 mL per mmol) and water (33 equiv.) a solution of PhSeCl (1 equiv.) in acetonitrile (1 mL per mmol) was added via cannula. After 3 minutes the reaction was quenched by addition of a saturated aqueous solution of NaHCO$_3$ and the mixture was partitioned between ethyl acetate and water. The combined organic phases were washed with brine and dried. The crude product was purified by flash chromatography.

(±)-(1RS, 2SR, 3RS)-1-phenyl-2-phenylselenenyl-butan-1,3-diol (2a): Mixture with 3a. From light petroleum/diethyl ether 1:1; white solid, mp 52-53 °C; IR (nujol) v: 3350, 1570, 1490, 1470 cm$^{-1}$; $^1$H-NMR δ: 1.31 (d, J=5.7Hz, 3H, CH$_3$), 1.36 (d, J=6.0Hz, 3H, CH$_3$, 3a), 3.35 (dd, J=4.6 and 1.6Hz, 1H, CHSePh), 3.61 (dd, J=7.6 and 5.5Hz, 1H, CHSePh, 3a), 3.86 (br s, 2H, OH), 4.14-4.19 (m, 1H, CH$_3$CH), 5.02 (d, J=7.6Hz, 1H, CHPh, 3a), 5.15 (d, J=4.6Hz, 1H, CHPh), 7.21-7.35 (m, 8H, ArH), 7.49-7.56 (m, 2H, ArH); $^{13}$C-NMR δ: 21.9, 61.1, 66.8, 76.7, 126.0, 127.5, 128.1, 128.3, 129.1, 134.4, 141.9; Anal. Calcd. for C$_{16}$H$_{18}$O$_2$Se: C, 59.82; H, 5.65. Found: C, 60.39; H, 5.69.

(±)-(1RS, 2SR, 3RS)-4-methyl-1-phenyl-2-phenylselenenyl-pentan-1,3-diol (2b): Mixture with 3b. From light petroleum/diethyl ether 3:1; oil; IR (liquid film) v: 3300, 1455 cm$^{-1}$; $^1$H-NMR δ: 0.68 (d, J=6.6Hz, 3H, CH$_3$), 0.82 (d, J=6.7Hz, 3H, CH$_3$, 3b), 0.93 (d, J=6.7Hz, 3H, CH$_3$, 3b), 0.99 (d, J=6.7, 3H, CH$_3$), 2.05-2.21 (m, 1H, CHMe$_2$), 3.44 (dd, J=9.2 and 2.5Hz, 1H, CHSePh ), 3.56 (d, J=3.3Hz, 1H, OH), 3.60-3.66 (m, 1H, i-PrCHOH), 4.05 (d, J=4.5Hz, 1H, OH), 5.19-5.22 (m, 1H, CHPh), 7.21-7.44 (m, 8H, ArH), 7.65-7.69 (m, 2H, ArH); $^{13}$C-NMR δ: 18.7, 18.9, 32.2, 58.1, 75.9, 76.4, 125.6, 127.3, 127.7, 128.2, 129.2, 134.8, 141.3; Anal. Calcd. for C$_{18}$H$_{22}$O$_2$Se: C, 61.89; H, 6.35. Found: C, 62.57; H, 6.39.
(±)-(1RS, 2SR, 3RS)-1-p-chlorophenyl-2-phenylselenenyl-butan-1,3-diol (2e): Mixture with 3c. From light petroleum/diethyl ether 4:1; oil; IR (liquid film) ν: 3350, 1590, 1575, 1485, 1470 cm⁻¹; ¹H-NMR δ: 1.31 (d, J=6.3Hz, 3H, CH₃), 1.36 (d, J=6.2Hz, 3H, CH₃, 3c), 3.16 (dd, J=7.5 and 1.5Hz, 1H, CHSePh, overlapped with br s, 2H, OH), 4.13 (dq, J=6.3 and 1.3Hz, 1H, CH₃CH₂), 5.08 (d, J=4.7Hz, 1H, CHAr), 7.15-7.30 (m, 7H, ArH), 7.44-7.51 (m, 2H, ArH); ¹³C-NMR δ: 22.0, 61.1, 66.9, 76.1, 127.5, 127.8, 128.5, 129.2, 134.5, 140.3; Anal. Calcd. for C₁₆H₁₇ClO₂Se: C, 54.02; H, 4.82. Found: C, 54.40; H, 4.80.

(±)-(1RS, 3RS)-3-phenylselenenyl-pentan-1,3-diol (2d): Mixture with 3d. From light petroleum/diethyl ether 4:1; white solid, mp 52-53 °C; IR (nujol) ν: 3300, 1570, 1450 cm⁻¹; ¹H-NMR δ: 1.36 (d, J=6.5Hz, 3H, CH₃), 1.40 (d, J=6.3Hz, 3H, CH₃), 3.15 (dd, J=5.0 and 2.7Hz, 1H, CHSePh), 3.57 (br s, 2H, OH), 4.18 (dq, J=6.5 and 5.0Hz, 1H, CHOH), 4.33 (dq, J= 6.3 and 2.7Hz, 1H, CHOH ), 7.25-7.30 (m, 3H, ArH), 7.55-7.62 (m, 2H, ArH); ¹³C-NMR δ: 21.5, 62.2, 67.1, 69.8, 127.4, 129.1, 129.5, 134.0; Anal. Calcd. for C₁₁H₁₆O₂Se: C, 50.97; H, 6.22. Found: C, 51.10; 6.30.

(±)-(1RS, 3RS)-1,3-diphenyl-2-phenylselenenyl-propan-1,3-diol (2e): From light petroleum/diethyl ether 4:1; white solid, mp 137-138 °C; IR (nujol) ν: 3400, 1596, 1490, 1470, 1445, 1430 cm⁻¹; ¹H-NMR δ: 3.56 (dd, J=3.9 and 1.7Hz, 1H, CHSePh overlapped with br s, 1H, OH), 3.63 (br s, 1H, OH), 5.13 (d, J=1.7Hz, 1H, CHOH), 5.20 (d, J= 3.9Hz, 1H, CHOH), 7.10-7.40 (m, 15H, ArH); ¹³C-NMR δ: 63.4, 71.5, 76.5, 125.7, 125.8, 127.2, 127.5, 127.7, 127.9, 128.5, 128.9, 134.4, 134.5, 141.3, 142.0; Anal. Calcd. for C₂₁H₂₀O₂Se: C, 65.80; H, 5.26. Found: 66.60; H, 5.31.

General procedure for azido-selenenylation reactions:

To a stirred solution of PhSeCl (1 equiv.), NaN₃ (5 equiv.) and AgOTf (1 equiv.) in DMSO (74 mL per mmol of PhSeCl) a solution of compounds 1a-f in DMSO (4.4 mL per mmol) was added via cannula. After 24 hours the reaction was quenched by addition of water and the mixture was portioned between diethyl ether and water. The combined organic phases were washed with brine and dried. The crude product was purified by flash chromatography.

(±)-(2RS, 3RS)-4-azido-4-phenyl-3-phenylselenenyl-butan-2-ol (4a): From light petroleum/diethyl ether 9:1; white solid, mp 62-63 °C; IR (nujol) ν: 3270, 2090 cm⁻¹; ¹H-NMR δ: 1.43 (d, J=6.3Hz, 3H, CH₃), 2.51 (br s, 1H, OH), 3.25 (dd, J=6.1 and 1.4Hz, 1H, CHSePh), 4.31 (dq, J=6.3 and 1.4Hz, 1H, CH₃CH₂), 4.93 (d, J=6.1Hz, 1H, CHPh), 7.16-7.37 (m, 10H, ArH); ¹³C-NMR δ: 22.4, 60.8, 66.2, 68.9, 127.5, 127.7, 128.4, 128.5, 129.9, 134.7, 137.8; Anal. Calcd. for C₁₆H₁₇N₃OSe: C, 55.49; H, 4.95. Found: 55.90; H, 5.05.

(±)-(2RS, 3SR, 4SR)-4-azido-4-phenyl-3-phenylselenenyl-butan-2-ol (5a): From light petroleum/diethyl ether 9:1; white solid, mp 87-88 °C; IR (nujol) ν: 3400, 2090 cm⁻¹; ¹H-NMR δ: 1.31 (d, J=6.3Hz, 3H, CH₃), 2.40 (br s, 1H, OH), 3.53 (dd, J=9.7 and 4.5Hz, 1H, CHSePh), 4.10-4.20 (m, 1H, CH₃CH₂), 4.76 (d, J=9.7Hz, 1H, CHPh), 7.05-7.29 (m, 10H, ArH); ¹³C-NMR δ: 20.6, 62.8, 66.9, 68.3, 127.7, 127.0,
128.4, 128.6, 128.9, 129.0, 134.6, 137.2; Anal. Calcd. for C_{16}H_{17}N_{3}OSe: C, 55.49; H, 4.95. Found: C, 56.09; H, 5.06.

(±)-(2RS, 3RS, 4RS)-5-azido-2-methyl-5-phenyl-4-phenylselenenyl-pentan-3-ol (4b): Mixture with 5b. From light petroleum/diethyl ether 9:1; white solid, mp 68-71 °C; IR (nujol) ν: 3500, 2090, 1575 cm⁻¹; ¹H-NMR δ: 0.81 (d, J=6.6Hz, 3H, CH₃), 0.84 (d, J=6.7Hz, 3H, CH₃, 5b), 1.04 (d, J=6.7Hz, 3H, CH₃, 5b), 1.14 (d, J=6.6Hz, 3H, CH₃), 2.18-23 (m, 1H, CHMe₂), 2.70 (br s, 1H,OH), 3.56 (dd, J=7.2 and 0.8Hz, 1H, CHSePh), 3.64-3.68 (m, 1H, CHOCH), 5.03 (d, J=7.2Hz, 1H, CHPh), 5.25 (d, J=7.4Hz, 1H, CHPh, 5b), 7.23-7.50 (m, 10H, ArH); ¹³C-NMR δ: 18.9, 19.1, 32.2, 57.2, 69.1, 75.6, 127.4, 127.7, 128.2, 128.5, 128.9, 135.0, 138.0; Anal. Calcd. for C_{18}H_{21}N_{3}OSe: C, 57.75; H, 5.65. Found: C, 58.23; H, 5.80.

(±)-(2RS, 3RS, 4RS)-4-azido-4-p-chlorophenyl-3-phenylselenenyl-butan-2-ol (4c): From light petroleum/diethyl ether 3:1; white solid, mp 54-55 °C; IR (nujol) ν: 3500, 2090 cm⁻¹; ¹H-NMR δ: 1.47 (d, J=6.2Hz, 3H, CH₃), 2.49 (br s, 1H, OH), 3.23 (dd, J=8.5 and 1.3Hz, 1H, CHSePh), 4.33 (dq, J=6.2 and 1.3Hz, 1H, CH₃CH₂), 4.90 (d, J=8.5Hz, 1H, CHAr), 7.10-7.28 (m, 9H, ArH); ¹³C-NMR δ: 22.6, 60.7, 88.2, 68.2, 127.7, 129.0, 129.1, 134.6, 136.4; Anal. Calcd. for C_{16}H_{16}ClN_{3}OSe: C, 50.47; H, 4.24. Found: C, 51.01; H, 4.34.

(±)-(2RS, 3RS, 4RS)-4-azido-3-phenylselenenyl-pentan-2-ol (4d): Mixture with 5d. From light petroleum/diethyl ether 7:1; oil; IR (liquid film) ν: 3430, 2100, 1575 cm⁻¹; ¹H-NMR δ: 1.30 (d, J=6.4Hz, 3H, CH₃, 5d), 1.41 (d, J=6.3Hz, 3H, CH₃), 1.47 (d, J=6.8Hz, 3H, CH₃), 2.68 (br s, 1H, OH), 3.32 (dd, J=7.8 and 1.9Hz, 1H, CHSePh), 3.26 (dd, J=7.0 and 5.8Hz, 1H, CHSePh, 5d), 3.91 (dq, J=6.8 and 6.5Hz, 1H, CH₃), 4.21 (dq, J=6.3 and 2.5Hz, 1H, CHAr), 7.10-7.28 (m, 9H, ArH); ¹³C-NMR δ: 62.6, 69.0, 71.4, 126.0, 127.4, 127.5, 127.6, 128.5, 128.3, 129.1, 134.6, 136.4; Anal. Calcd. for C_{11}H_{15}N_{3}OSe: C, 46.48; H, 5.32. Found: C, 46.90; H, 5.40.

(±)-(2RS, 3RS, 4RS)-3-azido-1,3-di phenyl-2-phenylselenenyl-propan-1-ol (4e): From light petroleum/diethyl ether 15:1; white solid, mp 77-78 °C; IR (nujol) ν: 3400, 2100 cm⁻¹; ¹H-NMR δ: 2.94 (br s, 1H, OH), 3.38 (dd, J=7.8 and 1.9Hz, 1H, CHSePh), 5.00 (d, J=7.8Hz, 1H, CHPh), 5.33 (d, J=1.9Hz, 1H, CHPh), 6.8-6.82 (m, 2H, ArH), 7.11-7.17 (m, 1H, ArH), 7.23-7.37 (m, 10H, ArH); ¹³C-NMR δ: 62.6, 69.0, 71.4, 126.0, 127.4, 127.5, 127.6, 128.1, 128.5, 128.6, 128.7, 134.8, 137.8, 142.2; Anal. Calcd. for C_{21}H_{19}N_{3}OSe: C, 61.77; H, 4.69. Found: C, 62.10; H, 4.74.

(±)-(3RS, 4RS, 5RS)-5-azido-3-hydroxy-4-phenylselenenyl-5-phenyl-pentanoate ethyl ester (4f): From light petroleum/diethyl ether 3:1; white solid, mp 92-93 °C; IR (nujol) ν: 3400, 2100, 1575 cm⁻¹; ¹H-NMR δ: 2.94 (br s, 1H, OH), 3.38 (dd, J=7.8 and 1.9Hz, 1H, CHSePh), 5.00 (d, J=7.8Hz, 1H, CHPh), 5.33 (d, J=1.9Hz, 1H, CHPh), 6.8-6.82 (m, 2H, ArH), 7.11-7.17 (m, 1H, ArH), 7.23-7.37 (m, 10H, ArH); ¹³C-NMR δ: 126.0, 127.4, 127.5, 127.6, 128.1, 128.5, 128.6, 128.7, 134.8, 137.8, 142.2; Anal. Calcd. for C_{19}H_{21}N_{3}OSe: C, 61.77; H, 4.69. Found: C, 62.10; H, 4.74.
(±)-(2RS, 3RS, 4RS)-4-azido-5-phenyl-3-phenylselenenyl-pentan-2-ol (4g): From light petroleum/diethyl ether 10:1; oil; IR (liquid film) ν: 3330, 2100 cm⁻¹; ¹H-NMR δ: 1.43 (d, J=6.3 Hz, 3H, CH₃), 2.59 (br s, 1H, OH), 2.92 (dd, J=13.8 and 8.8Hz, 1H, PhCHH), 3.11 (dd, J=5.3 and 1.8Hz, 1H, CHSePh), 3.22 (dd, J=13.8 and 5.4Hz, 1H, PhCHH), 3.97-4.05 (m, 1H, CHN₃), 4.34 (dt, J=6.3 and 1.8Hz, 1H, CHOH), 7.11-7.15 (m, 2H, ArH), 7.25-7.32 (m, 6H, ArH), 7.46-7.50 (m, 2H, ArH); ¹³C-NMR δ: 22.4, 39.7, 58.4, 66.4, 67.7, 126.9, 127.5, 128.7, 129.1, 129.3, 133.9, 137.1; Anal. Calcd. for C₁₇H₁₉N₃OSe: C, 56.67; H, 5.32. Found: C, 56.99; H, 5.35.

(±)-(2RS, 3SR, 4SR)-4-azido-5-phenyl-3-phenylselenenyl-pentan-2-ol (5g): From light petroleum/diethyl ether 10:1; oil. IR (liquid film) ν: 3370, 2100 cm⁻¹; ¹H-NMR δ: 1.35 (d, J=6.3Hz, 3H, CH₃), 2.29 (br s, 1H, OH), 2.75 (dd, J=13.9 and 9.9Hz, 1H, PhCHH), 3.36 (dd, J=7.2 and 5.3Hz, 1H, CHSePh), 3.43 (dd, J=13.9 and 3.6Hz, 1H, PhCHH), 3.89 (ddd, J=9.9, 7.2 and 3.6Hz, 1H, CHN₃), 4.34 (dt, J=6.3 and 5.3Hz, 1H, CHOH), 7.20-7.35 (m, 8H, ArH), 7.59-7.63 (m, 2H, ArH); ¹³C-NMR δ: 21.4, 39.8, 60.8, 66.5, 67.6, 126.9, 128.0, 128.7, 129.3, 129.5, 134.1, 137.6; Anal. Calcd. for C₁₇H₁₉N₃OSe: C, 56.67; H, 5.32. Found: C, 57.05; H, 5.41.

(±)-(4RS, 5RS, 6RS)-6-methyl-4-phenyl-5-phenylselenenyl-1,3-oxazolidin-2-one (9)

To a solution of compound 4a (100 mg, 0.298 mmol) in dry THF (6 mL), PPh₃ (84 mg, 1.1 equiv.) was added. The solution was stirred at 40 °C overnight. After this time, water (0.30 mL) was added and the solution stirred at 50 °C for 3 h. Methanol was then added and the solution evaporated under reduced pressure. The residue was dessicated under vacuum in the presence of P₂O₅ for 5 h. The white residue obtained was used without further purification in the next step. The residue (95 mg) was dissolved in CH₂Cl₂ (2 mL) at 0 °C then 1,1'-carbonyldiimidazole (58 mg, 0.36 mmol) was added. The solution was allowed to warm at room temperature then stirred for 48 h. After this time the solvent was removed under reduced pressure and the residue purified by flash chromatography using CH₂Cl₂/ethyl acetate 7:1 as eluent to afford compound 9 (34 mg, 34%) as yellow solid, m.p. 175-177 °C; IR (nujol) ν: 3350, 1720, 1690, 1455 cm⁻¹; ¹H-NMR δ: 1.50 (d, J=6.4 Hz, 3H, CH₃), 3.44-3.46 (m, 1H, CHSePh), 4.55 (dt, J=6.4 and 2.5 Hz, 1H, CHCH₃), 4.72 (dd, J=3.6 Hz, 1H, CHPh), 5.81 (d, J=3.6 Hz, 1H, NH), 7.12-7.16 (m, 2H, ArH), 7.27-7.37 (m, 6H, ArH), 7.52-7.56 (m, 2H, ArH); ¹³C-NMR δ: 18.8, 49.1, 59.4, 72.0, 126.3, 128.3, 128.6, 128.9, 129.5, 135.4, 140.5, 153.5.

Hydroxy-selenenylation reaction of compound 10

To a stirred solution of compound 10 (100 mg, 0.58 mmol) in acetonitrile (1 mL) and water (340 µL) a solution of PhSeCl (110 mg, 1 equiv.) in acetonitrile (0.8 mL) was added via cannula. After 3 minutes the reaction was quenched by addition of a saturated aqueous solution of NaHCO₃ and the mixture was portioned between diethyl ether and water. The combined organic phases were washed with brine and dried. The crude product was purified by flash chromatography to give (±)-(1RS, 2SR, 3RS)-3-azido-1-phenyl-2-phenylselenenyl-butan-1-ol (11) as a mixture with 12. From light petroleum/diethyl ether 9:1; oil; IR (liquid film) ν: 3430, 2100, 1575 cm⁻¹; ¹H-NMR δ: 1.44 (d, J=6.5Hz, 3H, CH₃, 12), 1.52 (d, J=6.5 Hz, 3H, CH₃), 2.95 (d, J=3.1 Hz, 1H, OH), 3.19 (dd, J=7.5 and
Oxidation of compound 4a

To a solution of compound 4a (100 mg, 0.312 mmol) in methanol (3 mL) at -10 °C was added K$_2$CO$_3$ (261 mg). After 10 min m-chloroperbenzoic acid (269 mg, 1.56 mmol) was added. The reaction was quenched by adding water then the solution was partitioned between water and diethyl ether. The organic phase was washed with Na$_2$S$_2$O$_3$, dried and evaporated under reduced pressure. Purification by flash chromatography with light petroleum/diethyl ether 4/1 gave (±)-(2SR, 3RS, 4RS)-4-azido-4-phenyl-butan-2,3-oxirane (14) as an oil; IR (liquid film) ν: 2090, 1620 cm$^{-1}$; $^1$H-NMR δ: 1.42 (d, J=5.6Hz, 3H, CH$_3$), 3.10-3.19 (m, 1H), 3.25 (dd, J=8.8 and 4.2Hz, 1H), 4.39 (d, J=8.8Hz, 1H), 7.32-7.45 (5H, ArH); $^{13}$C-NMR δ: 13.8, 52.4, 59.5, 64.6, 126.8, 128.8, 129.0, 136.0; Anal. Calcd. for C$_{10}$H$_{11}$N$_3$O: C, 63.48; H, 5.86. Found: C, 64.10; H, 5.92.

(Z)-4-azido-4-phenyl-but-3-en-2-ol (13) was obtained following the same procedure but using 1.2 equivalents of K$_2$CO$_3$ and MCPBA: Yellow oil; IR (liquid film) ν: 3420, 2100, 1638 cm$^{-1}$; $^1$H-NMR δ: 1.34 (d, J=6.4Hz, 3H, CH$_3$), 2.00 (br s, 1H, OH), 4.85 (dt, J=7.8 and 6.4Hz, 1H), 5.22 (d, J=7.8Hz, 1H), 7.36-7.45 (5H, ArH); Anal. Calcd. for C$_{10}$H$_{11}$N$_3$O: C, 63.48; H, 5.86. Found: C, 64.00; H, 5.90.

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Sample availability: Available from the authors.

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