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1,4-Asymmetric Induction in Methoxyselenenylation of Double Bonds at the Nitrogen Side of Chiral Perhydro-1,3-benzoxazines Promoted by Nonbonded Se···N Interactions

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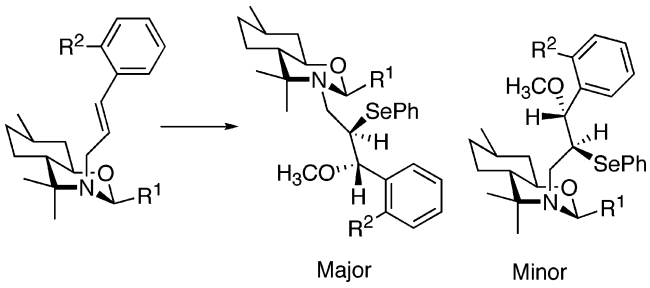

Regio- and diastereoselective methoxyselenenylation of cinnamylamines attached to a chiral perhydrobenzoxazine occurs in high yields by reaction with benzeneselenenyl chloride in dichloromethane−methanol. The diastereoselection is dependent on the temperature of the reaction and the structure of the substituent at C-2 and can be rationalized by accepting a 1,4-asymmetric induction process after coordination of the selenium to the nitrogen atom of the allylamine system.

Nonbonded interactions between a divalent selenium atom and an electron donor heteroatom play a significant role in different fields, such as the activity of therapeutic agents,[1] the catalytic mechanism of glutathione peroxidase mimics,[2] and the stabilization of unstable organoselenium compounds.[3] These interactions are also responsible for the origin of the stereoselectivity in asymmetric synthesis using chiral selenium compounds[4] and the design of new chiral reagents.[5] Furthermore, these nonbonded interactions, which are derived from the hypervalent nature of the selenium, can dramatically influence the regio- and stereochemical outcome of selenenylation and selenocyclization reactions due to the interaction of the selenium electrophiles with nearby heteroatoms or external additives.[6] Consequently, systematic structural investigations on the origin, magnitude, and theoretical interpretation of such interactions that involve Se···N,[7] Se···O,[8] and Se···X[9] (X = halogen) atoms have been carried out.

We have previously described the regio- and diastereoselective methoxyselenenylation of 2-vinylperhydro-1,3-benzoxazines,[10] and the high diastereoselectivities observed were imputed to nonbonded interactions between the selenium and the oxygen atom of the oxazine ring. Nevertheless, since Se···N interactions are also possible,[7] we envisioned that the stereoselection of the methoxyselenenylation of an allyl substituent placed at the nitrogen side of a chiral perhydrobenzoxazine can be greatly improved due to nonbonded interactions between the selenium of an incoming electrophile and the nitrogen atom of the *N*-allyl substituent. Stereoselective electrophilic selenenylation of allylic alcohol derivatives has been previously described,[11] but to our knowledge, this is the first example of stereoselective methoxyselenenylation of allylic amines.[12]

With this purpose, perhydro-1,3-benzoxazines **4a**−**i**, which essentially differ in the nature and size of the substituent at the N,O-ketalic carbon of the heterocycle, were prepared as summarized in Scheme 1.

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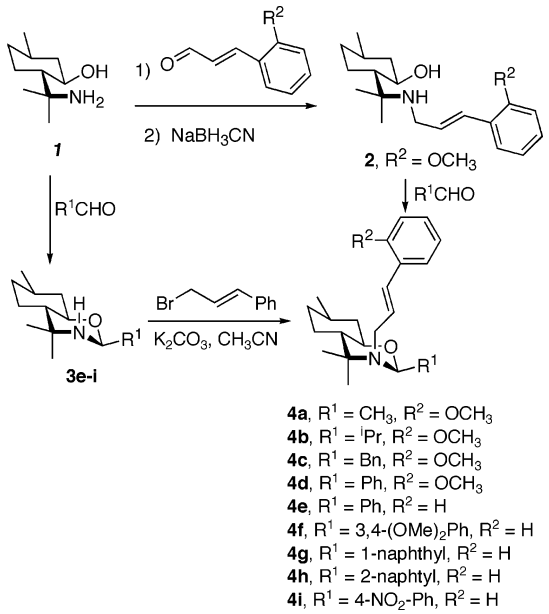
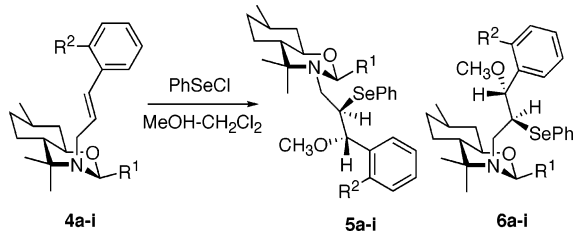
SCHEME 1. Synthesis of Chiral *N*-Allyl Perhydrobenzoxazines 4a−i



SCHEME 2. Methoxyselenenylation of Compounds 4a−i



The *o*-methoxy cinnamyl derivatives **4a**−**d** were prepared in three steps by condensation of *o*-methoxycinnamaldehyde with (−)-8-aminomenthol to the corresponding oxazine[13] and were transformed into the amino alcohol **2** (92%) by reduction with sodium cyanoborohydride in methanol under slightly acidic conditions. This amino alcohol was converted into the final perhydro-1,3-benzoxazines **4a**−**d** (80−86%) by heating with acetaldehyde or isobutyraldehyde at 80 °C in a sealed tube for **4a** and **4b**, or by heating with phenylacetaldehyde or benzaldehyde in refluxing toluene for **4c** and **4d**. The *N*-cinnamyl derivatives **4e**−**i** were prepared in two steps by condensation of (−)-8-aminomenthol **1** with the corresponding aldehyde in refluxing toluene, leading nearly quantitatively to oxazines **3e**−**i**, which were alkylated with cinnamyl bromide and K_2CO_3 in acetonitrile to **4e**−**i** (80−88%).

Methoxyselenenylation of **4a**−**i** was carried out employing benzeneselenenyl chloride as electrophilic reagent,[14] in a 4/1 mixture of MeOH/CH_2Cl_2 at room temperature or at −15 °C. The results are summarized in Scheme 2 and Table 1.

Methoxyselenenylation of cinnamylamine **4a** at room temperature led to **5a** and **6a** with excellent yield, but with modest stereoselectivity (entry 1 in Table 1). When the reaction temperature was lowered to −15 °C, the reaction time increased but the chemical yield remained excellent, and the diastereoselectivity improved to 68:32 (entry 2). In the same conditions,

TABLE 1. Methoxyselenenylation of Cinnamylamines 4a−i

entry	compound	R^1	R^2	*T* (°C)	yield (%)[a]	product ratios (%)[b]
1	**4a**	CH_3	OCH_3	22	93	**5a** (57), **6a** (43)
2	**4a**	CH_3	OCH_3	−15	92	**5a** (68), **6a** (32)
3	**4b**	*i*Pr	OCH_3	22	90	**5b** (78), **6b** (22)
4	**4b**	*i*Pr	OCH_3	−15	91	**5b** (>96)[c]
5	**4c**	Bn	OCH_3	−15	93	**5c** (56), **6c** (44)
6	**4d**	Ph	OCH_3	22	85	**5d** (86), **6d** (14)
7	**4d**	Ph	OCH_3	−15	91	**5d** (94), **6d** (6)
8	**4e**	Ph	H	22	92	**5e** (85), **6e** (15)
9	**4e**	Ph	H	−15	90	**5e** (92), **6e** (8)
10	**4f**	3,4-$(OCH_3)-C_6H_3$	H	−15	87	**5f** (95), **6f** (5)
11	**4g**	1-naphthyl	H	−15	88	**5g** (74), **6g** (26)
12	**4h**	2-naphthyl	H	−15	90	**5h** (>96)[c]
13	**4i**	4-$NO_2-C_6H_4$	H	−15	78	**5i** (80), **6i** (20)

[a] Chemical yield refers to pure compounds after column chromatography. [b] Determined by ^{1}H NMR of the reaction mixtures. [c] Only one diastereoisomer was detected by ^{1}H NMR.

methoxyselenenylation of allylamine **4c** with a benzylic group at C-2 of the benzoxazine ring showed a very low degree of stereoselection, and **5c** and **6c** were obtained as an almost equimolar mixture of diastereoisomers (entry 5). In contrast, **4b** with a bulkier isopropyl group at C-2 reacted at −15 °C with total diastereoselectivity, leading a single diastereoisomer **5b** in excellent yield (entry 4), although at room temperature the diastereomeric excess decreased significantly (entry 3).

The behavior of **4d** and **4e** with a phenyl group at C-2 of the heterocycle is very similar, and methoxyselenenylation at −15° C turned out also with high yield and stereoselectivity (entries 7 and 9), although the latter decreases at room temperature (entries 6 and 8).

The good level of stereoselection was maintained for methoxyselenenylation of benzoxazines **4f** and **4h** with a 3,4-dimethoxyphenyl and 2-naphthyl group, respectively (entries 10 and 12), but surprisingly, the diastereomeric ratio decreased for benzoxazines **4g** and **4i** with similar bulky 1-naphthyl or 4-nitrophenyl substituents at C-2 (entries 11 and 13).

The diastereoisomers formed in each reaction were separated by flash chromatography (except the mixture of **5c** and **6c**, and the minor products **6b** and **6f** that were not obtained pure), and the regiochemistry was determined on the basis of the ^{1}H and ^{13}C NMR data, whereas the absolute stereochemistry of **5a**, **5d**,[15] and the minor product **6a**[10] was established by X-ray diffraction analysis.

The interatomic distances between the Se and the N atoms in the oxazine rings for **5a**, **5d**, and **6a** are 3.008, 3.205, and 2.850 Å, respectively. These distances are shorter than the sum of van der Waal's radii (3.5 Å), and they might indicate a weak secondary interaction between both selenium and nitrogen atoms. The coordination geometry around the selenium atom is distorted T-shaped, and the substituent at the nitrogen atom is equatorially oriented in compounds **5a** and **5d** but in axial arrangement in product **6a**.

Both the presence of a nonbonded Se···N interaction and the stereocenter at C-2 in the perhydrobenzoxazines is essential for good diastereoselectivities. In this way, we observed that the reaction of the open (−)-8-amino menthol derivative **2** with phenylselenyl chloride in any of the reaction conditions described yielded an equimolar mixture of diastereoisomers. In

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(14) The use of different electrophilic reagents, such as PhSeBr or PhSeOTf, did not improve the results obtained with PhSeCl.

(15) Crystallographic data can be obtained from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EZ, UK. E-mail: deposit@ccdc.cam.ac.uk.

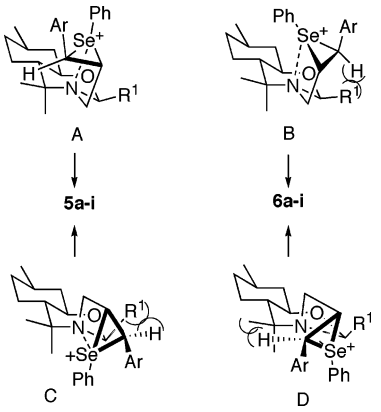

FIGURE 1. Proposed plausible seleniranium intermediates.

addition, when **4d** hydrochloride was subjected to methoxyselenenylation at room temperature, an almost equimolar mixture of diastereoisomers **5d** (54%) and **6d** (46%) was obtained in 80%. In this case, the protonated nitrogen is unable to interact with the selenium atom, and the reaction occurred without stereoselection. An additional experiment to test the change in the diastereoselection was made in the presence of an amine which is able to coordinate to the reagent, but **4e** was unable to react at room temperature with the complex formed from trithylamine and benzeneselenenyl chloride.

The excellent 1,4-asymmetric induction observed is noteworthy and can be explained as a consequence of the nonbonded Se···N interaction that forces the substituent of the chiral center at C-2 of the benzoxazine to come close to the seleniranium ion intermediate. After coordination of the selenium reagent, the nitrogen atom became a chiral center, and four possible intermediates can be envisaged (Figure 1): two intermediates, **A** and **B**, with the nitrogen substituent oriented in equatorial disposition and two intermediates, **C** and **D**, with the same substituent oriented in axial disposition. When R^1 is a methyl or a benzyl group, intermediates **A** or **B** and **C** or **D** are similarly hindered, and the facial discrimination is poor. However, when R^1 is a bulkier substituent, such as isopropyl or aryl groups, intermediates **B** and **C** are sterically less favorable due to the steric hindrance between the olefinic hydrogen and the substituent R^1, and no products were formed from these conformations. On the other hand, the substituent attached to the nitrogen atom is in axial conformation in the most stable conformation of perhydrobenzoxazines due to the generalized anomeric effect.[16] Nevertheless, the coordination of the selenium atom to the unshared electron pair of the nitrogen will destroy these effects, and the substituent attached to the nitrogen atom will prefer a less hindered equatorial arrangement, so that intermediate **A** is clearly favored.

The presence of a nonbonded Se···N interaction is essential to achieve good diastereoselectivities because methoxyselenenylation of **4d** hydrochloride leads to an almost equimolar mixture of diastereoisomers **5d** (54%) and **6d** (46%). The quaternary nitrogen in the salt cannot interact with the selenium atom, and the reaction showed a very low degree of stereoselection.

In summary, cinnamylamines taking part in a chiral perhydrobenzoxazine are regio- and stereoselectively functionalized by reaction with benzeneselenenyl chloride and methanol. When a mixture of diastereoisomers was formed, they were easily separated by column chromatography. This unprecedented transformation is a novel example of 1,4-asymmetric induction promoted by the stereocenter placed at C-2 in the perhydrobenzoxazine system.

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Experimental Section

Methoxyselenenylation of Allylamines 4a−i. General Method. To a stirred mixture of benzeneselenenyl chloride (1.1 g, 5.7 mmol) in methanol (20 mL) was added a solution of the oxazines **4a−i** (5.2 mmol) in CH_2Cl_2 (5 mL). The solution was stirred at the temperature shown in Table 1 until the reaction was completed (TLC) and then diluted with a 10% aqueous solution of NaOH. The solvents were removed under reduced pressure, and the aqueous phase was extracted with chloroform (3 × 30 mL). The combined organic extracts were washed with H_2O, dried over $MgSO_4$, the solvent was removed under reduced pressure, and the residue was chromatographed on silica gel using mixtures of hexane/EtOAc as eluent.

(2*S*,4a*S*,7*R*,8a*R*)-3-[(2*R*,3*S*)-3-Methoxy-3-(2-methoxyphenyl)-2-phenylselenylpropyl]-2,4,4,7-tetramethyloctahydrobenzo[*e*]-[1,3]oxazine (5a). Colorless solid. Mp: 165−166 °C (from EtOH). $[\alpha]^{25}_D = -12.0$ ($c = 1.0$, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 333 K): δ 0.72−0.99 (m, 3H), 0.74 (s, 3H), 0.79 (d, 3H, $J = 6.5$ Hz), 0.91 (s, 3H), 1.07 (m, 1H), 1.15 (d, 3H, $J = 5.8$ Hz), 1.21−1.40 (m, 2H), 1.52 (m, 1H), 1.75 (m, 1H), 2.54 (dd, 1H, $J_1 = 16.1$ Hz, $J_2 = 3.3$ Hz), 3.07 (dd, 1H, $J_1 = 16.1$ Hz, $J_2 = 11.6$ Hz), 3.18 (s, 3H), 3.23 (td, 1H, $J_1 = 10.5$ Hz, $J_2 = 4.0$ Hz), 3.55 (s, 3H), 3.70 (ddd, 1H, $J_1 = 11.6$ Hz, $J_2 = 3.3$ Hz, $J_3 = 2.8$ Hz), 4.47 (q, 1H, $J = 5.8$ Hz), 4.69 (d, 1H, $J = 2.8$ Hz), 6.68 (d, 1H, $J = 8.2$ Hz), 6.86 (t, 1H, $J = 7.5$ Hz), 7.08−7.16 (m, 4H), 7.29 (d, 1H, $J = 7.5$ Hz), 7.60−7.65 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, 333 K): δ 19.4, 21.0, 22.1, 25.0, 26.2, 31.4, 35.1, 41.5, 41.6, 45.8, 53.9, 54.9, 57.4, 58.0, 75.9, 80.2, 84.1, 110.5, 120.3, 126.5, 127.1, 128.2, 128.3 (3C), 132.5, 134.8 (2C), 157.1. IR (Nujol): ν 3060, 3040, 1595, 1585, 760, 745, 650 cm^{-1}. Anal. Calcd for $C_{29}H_{41}NO_3Se$: C, 65.64; H, 7.79; N, 2.64. Found: C, 65.46; H, 7.64; N, 2.79.

(2*S*,4a*S*,7*R*,8a*R*)-2-Isopropyl-3-[(2*R*,3*S*)-3-methoxy-3-(2-methoxyphenyl)-2-phenylselenylpropyl]-4,4,7-trimethyloctahydrobenzo-[*e*][1,3]oxazine (5b). Colorless solid. Mp: 130−131 °C (from EtOH). $[\alpha]^{25}_D = -25.6$ ($c = 1.0$, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 333 K): δ 0.70−1.02 (m, 3H), 0.80 (d, 3H, $J = 6.5$ Hz), 0.85 (d, 3H, $J = 6.5$ Hz), 0.87 (d, 3H, $J = 6.5$ Hz), 0.93 (s, 3H), 0.97 (s, 3H), 1.21 (m, 1H), 1.28−1.54 (m, 3H), 1.61 (m, 1H), 1.80 (m, 1H), 2.57 (m, 1H), 3.02 (dd, 1H, $J_1 = 16.2$ Hz, $J_2 = 11.4$ Hz), 3.20 (td, 1H, $J_1 = 10.5$ Hz, $J_2 = 4.0$ Hz), 3.27 (s, 3H), 3.61 (s, 3H), 3.73−3.79 (m, 2H), 4.71 (d, 1H, $J = 2.5$ Hz), 6.75 (d, 1H, $J = 8.2$ Hz), 6.93 (t, 1H, $J = 7.5$ Hz), 7.15−7.27 (m, 4H), 7.36 (dd, 1H, $J_1 = 7.5$ Hz, $J_2 = 1.6$ Hz), 7.71−7.74 (m, 2H). ^{13}C NMR ($CDCl_3$, 333 K): δ 17.5, 18.4, 20.8, 22.1, 25.1, 27.0, 29.5, 31.3, 35.1, 41.4, 43.1, 46.8, 52.3, 54.7, 57.6, 58.1, 76.0, 80.4, 93.7, 110.2, 120.2, 126.5, 127.2, 128.0, 128.2, 128.3 (2C), 132.1, 134.7 (2C), 157.0. IR (Nujol): ν 3060, 1600, 1580, 780, 760, 710, 680 cm^{-1}. Anal. Calcd for $C_{31}H_{45}NO_3Se$: C, 66.65; H, 8.12; N, 2.51. Found: C, 66.72; H, 8.26; N, 2.62.

(2*S*,4a*S*,7*R*,8a*R*)-3-[(2*R*,3*S*)-3-Methoxy-3-(2-methoxyphenyl)-2-phenylselenylpropyl]-4,4,7-trimethyl-2-phenyloctahydrobenzo-[*e*][1,3]oxazine (5d). Colorless solid. Mp: 198−199 °C (from EtOH). $[\alpha]^{25}_D = +32.5$ ($c = 1.0$, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 0.87−1.18 (m, 3H), 0.89 (d, 3H, $J = 6.5$ Hz), 1.03 (s, 3H), 1.23 (s, 3H), 1.46 (m, 1H), 1.51 (m, 1H), 1.61−1.73 (m, 2H), 1.88 (m, 1H), 2.17−2.33 (m, 2H), 3.07 (s, 3H), 3.09 (m, 1H), 3.41 (s, 3H), 3.46 (m, 1H), 4.18 (d, 1H, $J = 1.7$ Hz), 4.83 (s, 1H), 6.63 (dd, 1H, $J_1 = 8.3$ Hz, $J_2 = 1.1$ Hz), 6.90 (t, 1H, $J = 7.6$ Hz), 7.02−7.28 (m, 10H), 7.43−7.47 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 22.1, 22.2, 25.1,

27.4, 31.0, 34.6, 41.2, 42.1, 49.0, 49.8, 53.9, 57.8 (2C), 74.8, 77.4, 90.8, 109.7, 119.4, 126.5 (2C), 127.1, 127.5 (3C), 128.1 (4C), 131.1, 134.8 (3C), 140.6, 156.4. IR (Nujol): ν 3050, 1600, 1590, 760, 740, 695 cm^{-1}. Anal. Calcd for $C_{34}H_{43}NO_3Se$: C, 68.90; H, 7.31; N, 2.36. Found: C, 68.79; H, 7.17; N, 2.52.

(2*S*,4a*S*,7*R*,8a*R*)-3-[(2*R*,3*S*)-3-Methoxy-3-phenyl-2-phenylselenylpropyl]-4,4,7-trimethyl-2-phenyloctahydrobenzo[*e*][1,3]-oxazine (5e). Colorless oil. $[\alpha]^{25}_D = +33.1$ ($c = 1.0$, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 0.79−1.01 (m, 2H), 0.89 (d, 3H, $J = 6.4$ Hz), 1.03 (s, 3H), 1.08 (m, 1H), 1.24 (s, 3H), 1.33 (m, 1H), 1.51 (m, 1H), 1.59−1.72 (m, 2H), 1.89 (m, 1H), 2.19−2.35 (m, 2H), 3.03 (m, 1H), 3.04 (s, 3H), 3.45 (td, 1H, $J_1 = 10.5$ Hz, $J_2 = 4.1$ Hz), 3.70 (d, 1H, $J = 2.2$ Hz), 4.90 (s, 1H), 6.71−6.77 (m, 2H), 7.05−7.32 (m, 11H), 7.33−7.42 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 14.0, 22.1, 25.0, 27.4, 31.0, 34.6, 41.2, 42.0, 48.8, 52.9, 57.7, 57.8, 74.9, 82.6, 90.5, 126.4 (3C), 126.7, 126.8, 127.7 (4C), 128.3, 128.5 (3C), 131.2, 134.5 (2C), 139.5, 140.4. IR (film): ν 3060, 3030, 2920, 1600, 1580, 1450, 910, 730, 700, 650 cm^{-1}. Anal. Calcd for $C_{33}H_{41}NO_2Se$: C, 70.44; H, 7.34; N, 2.49. Found: C, 70.39; H, 7.51; N, 2.32.

(2*S*,4a*S*,7*R*,8a*R*)-2-(3,4-Dimethoxyphenyl)-3-[(2*R*,3*S*)-3-methoxy-3-phenyl-2-phenylselenylpropyl]-4,4,7-trimethyloctahydrobenzo[*e*][1,3]oxazine (5f). Colorless solid. Mp: 138−139 °C (from EtOH). $[\alpha]^{25}_D = +14.7$ ($c = 1.0$, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 333 K): δ 0.79−0.96 (m, 2H), 0.83 (d, 3H, $J = 6.5$ Hz), 0.97 (s, 3H), 1.03 (m, 1H), 1.18 (s, 3H), 1.35 (m, 1H), 1.46 (m, 1H), 1.58−1.69 (m, 2H), 1.84 (m, 1H), 2.25 (dd, 1H, $J_1 = 14.9$ Hz, $J_2 = 4.4$ Hz), 2.35 (ddd, 1H, $J_1 = 11.5$ Hz, $J_2 = 4.4$ Hz, $J_3 = 3.1$ Hz), 2.97 (s, 3H), 3.01 (dd, 1H, $J_1 = 14.9$ Hz, $J_2 = 11.5$ Hz), 3.40 (td, 1H, $J_1 = 10.5$ Hz, $J_2 = 4.2$ Hz), 3.66 (s, 3H), 3.67 (d, 1H, $J = 3.1$ Hz), 3.80 (s, 3H), 4.80 (s, 1H), 6.46 (d, 1H, $J = 8.1$ Hz), 6.54 (d, 1H, $J = 8.1$ Hz), 6.71−6.75 (m, 2H), 6.94 (s, 1H), 7.02−7.13 (m, 6H), 7.28−7.31 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 13.2, 22.1, 25.0, 27.5, 30.9, 34.5, 41.2, 41.9, 49.1, 52.3, 55.3, 55.8, 57.7, 57.8, 74.8, 82.0, 90.6, 110.2, 111.0, 120.2, 126.1 (2C), 126.6 (2C), 127.7 (2C), 128.7 (2C), 131.2, 133.1, 134.0 (2C), 139.7, 148.1, 148.6. IR (Nujol): ν 3040, 1595, 750, 740, 705, 695 cm^{-1}. Anal. Calcd for $C_{35}H_{45}NO_4Se$: C, 67.51; H, 7.28; N, 2.25. Found: C, 67.38; H, 7.40; N, 2.10.

(2*S*,4a*S*,7*R*,8a*R*)-3-[(2*R*,3*S*)-3-Methoxy-3-phenyl-2-phenylselenylpropyl]-4,4,7-trimethyl-2-naphthalen-1-yl-octahydrobenzo-[*e*][1,3]oxazine (5g). Colorless solid. Mp: 164−165 °C (from EtOH). $[\alpha]^{25}_D = +7.6$ ($c = 1.0$, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 333 K): δ 0.80−1.07 (m, 2H), 0.83 (d, 3H, $J = 6.5$ Hz), 1.13 (m, 1H), 1.15 (s, 3H), 1.16 (s, 3H), 1.34 (m, 1H), 1.52−1.75 (m, 3H), 1.86 (m, 1H), 2.27 (m, 1H), 2.50 (m, 1H), 2.83 (s, 3H), 3.05 (dd, 1H, $J_1 = 15.6$ Hz, $J_2 = 11.2$ Hz), 3.46 (d, 1H, $J = 2.7$ Hz), 3.50 (td, 1H, $J_1 = 10.5$ Hz, $J_2 = 4.1$ Hz), 5.59 (s br, 1H), 6.52−6.55 (m, 2H), 6.69−6.74 (m, 2H), 6.88−7.05 (m, 8H), 7.24−7.33 (m, 2H), 7.60 (d, 1H, $J = 8.3$ Hz), 7.69 (m, 1H), 8.63 (m, 1H). ^{13}C NMR ($CDCl_3$, 333 K): δ 17.3, 22.1, 25.3, 27.5, 31.3, 35.0, 41.5, 43.1, 48.6, 53.1, 57.5, 58.5, 75.9, 83.5 (2C), 125.1, 125.2, 125.3, 125.4, 126.4, 126.5, 126.6 (2C), 126.7, 127.7, 127.8 (2C), 128.3 (2C), 128.4, 131.5, 131.9, 134.0, 134.2 (2C), 135.9, 139.8. IR (Nujol): ν 3040, 1600, 1580, 780, 750, 735, 705, 690 cm^{-1}. Anal. Calcd for $C_{37}H_{43}NO_2Se$: C, 72.53; H, 7.07; N, 2.29. Found: C, 72.67; H, 6.96; N, 2.42.

(2*S*,4a*S*,7*R*,8a*R*)-3-[(2*R*,3*S*)-3-Methoxy-3-phenyl-2-phenylselenylpropyl]-4,4,7-trimethyl-2-naphthalen-2-yl-octahydrobenzo-[*e*][1,3]oxazine (5h). Colorless oil. $[\alpha]^{25}_D = +11.9$ ($c = 1.1$, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 333 K): δ 0.77−0.98 (m, 2H), 0.83 (d, 3H, $J = 6.5$ Hz), 1.02 (s, 3H), 1.07 (m, 1H), 1.19 (s, 3H), 1.38 (m, 1H), 1.49 (m, 1H), 1.58−1.68 (m, 2H), 1.85 (m, 1H), 2.34 (ddd, 1H, $J_1 = 11.5$ Hz, $J_2 = 4.4$ Hz, $J_3 = 3.1$ Hz), 2.37 (dd, 1H, $J_1 = 15.3$ Hz, $J_2 = 4.4$ Hz), 2.85 (s, 3H), 3.00 (dd, 1H, $J_1 = 15.3$ Hz, $J_2 = 11.5$ Hz), 3.42 (td, 1H, $J_1 = 10.5$ Hz, $J_2 = 4.2$ Hz), 3.54 (d, 1H, $J = 3.1$ Hz), 5.07 (s, 1H), 6.35 (d, 1H, $J = 7.3$ Hz), 6.37 (d, 1H, $J = 7.3$ Hz), 6.41−7.07 (m, 5H), 7.10 (d, 1H, $J = 8.1$ Hz), 7.12 (d, 1H, $J = 7.8$ Hz), 7.29−7.38 (m, 3H), 7.42−7.57 (m, 4H), 7.68 (d, 1H, $J = 7.3$ Hz). ^{13}C NMR ($CDCl_3$): δ 13.9, 22.2, 25.9, 27.4, 31.0, 34.7, 41.2, 42.1, 49.0, 53.0, 57.7, 57.9, 75.0, 82.4, 90.8, 125.3, 125.8 (3C), 126.6 (3C), 127.2, 127.3 (2C), 127.7 (2C), 128.5 (2C), 128.7, 131.2, 132.7, 133.4, 134.3 (2C), 137.9, 139.4. IR (film): ν 3060, 2980, 2920, 2870, 1600, 1580, 740, 705, 695 cm^{-1}. Anal. Calcd for $C_{37}H_{43}NO_2Se$: C, 72.53; H, 7.07; N, 2.29. Found: C, 72.39; H, 7.19; N, 2.37.

(2*S*,4a*S*,7*R*,8a*R*)-3-[(2*R*,3*S*)-3-Methoxy-3-phenyl-2-phenylselenylpropyl]-4,4,7-trimethyl-2-(4-nitrophenyl)octahydrobenzo-[*e*][1,3]oxazine (5i). Colorless oil. $[\alpha]^{25}_D = +26.1$ ($c = 1.0$, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 333 K): δ 0.87−1.04 (m, 2H), 0.92 (d, 3H, $J = 6.5$ Hz), 1.10 (m, 1H), 1.15 (s, 3H), 1.19 (s, 3H), 1.39−1.53 (m, 2H), 1.63−1.75 (m, 2H), 1.89 (m, 1H), 2.43 (ddd, 1H, $J_1 = 11.6$ Hz, $J_2 = 4.2$ Hz, $J_3 = 3.0$ Hz), 2.58 (dd, 1H, $J_1 = 15.7$ Hz, $J_2 = 4.2$ Hz), 3.01 (dd, 1H, $J_1 = 15.7$ Hz, $J_2 = 11.6$ Hz), 3.06 (s, 3H), 3.48 (td, 1H, $J_1 = 10.5$ Hz, $J_2 = 4.2$ Hz), 3.93 (d, 1H, $J = 3.0$ Hz), 5.20 (s, 1H), 6.76−6.81 (m, 2H), 7.16−7.23 (m, 6H), 7.35−7.39 (m, 4H), 7.89 (d, 2H, $J = 8.8$ Hz). ^{13}C NMR ($CDCl_3$, 333 K): δ 16.6, 22.1, 25.1, 27.1, 31.2, 34.9, 41.4, 42.2, 47.8, 54.0, 57.7, 58.2, 75.8, 84.3, 89.1, 122.7 (2C), 126.6 (2C), 127.1, 127.2, 128.0 (2C), 128.8 (2C), 129.3 (2C), 131.4, 134.7 (2C), 140.0, 147.4, 147.5. IR (film): ν 3040, 3020, 1605, 1580, 1530, 740, 700 cm^{-1}. Anal. Calcd for $C_{33}H_{40}N_2O_4Se$: C, 65.23; H, 6.64; N, 4.61. Found: C, 65.40; H, 6.53; N, 4.50.

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Supporting Information Available: General experimental methods and physical and spectral characteristics for compounds **2**, **3e**−**i**, **4a**−**i**, and **6a**−**i**. Copies of Ortep representation of X-ray structure for compounds **5a** and **5d**, and table of selected bond lengths (Å) and bond angles (deg) for **5a**, **5d**, and **6a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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