SUPPORTING INFORMATION

**Regio- and Stereoselective Methoxyselenylation of Chiral 2-Vinyl
Perhydro-1,3-benzoxazines Promoted by Selenium-Heteroatom
Nonbonded Interactions.**

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General Methods: All reactions were carried out in anhydrous solvents, under argon atmosphere, and in oven-dried glassware. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) were registered in CDCl_3 as solvent and chemical shifts are given relative to TMS as internal reference. Specific rotations were determined on a digital polarimeter using a Na lamp and concentration is given in g per 100 mL. Melting points were determined in open capillary tubes and are uncorrected. Products were isolated by flash chromatography using silica gel 60 (230-240 mesh).

Perhydro-1,3-benzoxazines **3a-f** have been previously described.²⁷

Synthesis of Perhydrobenzoxazines 3g and 3h. A mixture of N-benzylaminomenthol (3.81 g, 14.62 mmol) and cinnamaldehyde or 2-methoxycinnamaldehyde (15 mmol) in toluene (50 mL) was refluxed until the reaction was completed (TLC). The solvent was evaporated under vacuum and the residue was chromatographed on silica gel using a mixture hexane/EtOAc 15/1 as eluent.

(2S,4aS,7R,8aR)-3-Benzyl-2-styryl-4,4,7-trimethyl-octahydro-benzo[e][1,3]oxazine (3g). Yield: 82%. Colorless solid. Mp. 121-122 °C (from EtOH). $[\alpha]_{\text{D}}^{25} = -61.7$ ($c = 1.1$, CHCl_3). ^1H NMR (δ): 0.94-1.05 (m, 2H); 0.96 (d, 3H, $J = 6.5$ Hz); 1.08 (s, 3H); 1.15 (m, 1H); 1.25 (s, 3H); 1.45-1.65 (m, 2H); 1.66-1.74 (m, 2H); 1.99 (m, 1H); 3.60 (dt, 1H, $J_1 = 4.0$ Hz, $J_2 = 10.4$ Hz); 3.68 (d, 1H, $J = 17.1$ Hz); 4.07 (d, 1H, $J = 17.1$ Hz); 5.24 (d, 1H, $J = 4.7$ Hz); 5.91 (dd, 1H, $J_1 = 4.7$ Hz, $J_2 = 16.0$ Hz); 6.67 (d, 1H, $J = 16.0$ Hz); 7.03-7.06 (m, 2H); 7.11-7.25 (m, 6H); 7.33-7.35 (m, 2H). ^{13}C RMN (δ): 18.9; 22.2; 25.0; 27.2; 31.3; 34.9; 41.3; 46.7; 47.6; 56.8; 75.7; 87.7; 125.6; 126.5 (2C); 127.2 (2C); 127.; 127.9 (2C); 128.1 (2C); 129.4; 131.7; 136.6; 143.9. IR (Nujol): 3070, 3040, 1600, 750, 725, 715, 705 cm^{-1} . Anal. Calcd for $\text{C}_{23}\text{H}_{33}\text{NO}$: C, 83.15; H, 8.86; N, 3.73. Found: C, 83.06; H, 8.76; N, 3.89.

(2S,4aS,7R,8aR)-3-Benzyl-2-[2-trans-(2-methoxy-phenyl)-vinyl]-4,4,7-trimethyl-octahydro-benzo[e][1,3]oxazine (3h). Yield: 80%. Colorless solid. Mp. 91-92 °C (from EtOH). $[\alpha]_{\text{D}}^{25} = -70.2$ ($c = 1.1$, CHCl_3). ^1H NMR (δ): 0.89-1.03 (m, 2H); 0.95 (d, 3H, $J = 6.5$ Hz); 1.07 (s, 3H); 1.18 (m, 1H); 1.23 (s, 3H); 1.52-1.59 (m, 2H); 1.65-1.73 (m, 2H); 1.98 (m, 1H); 3.58 (td, 1H, $J_1 = 10.4$ Hz, $J_2 = 4.2$ Hz); 3.67 (d, 1H, $J = 17.1$ Hz); 3.73 (s, 3H); 4.07 (d, 1H, $J = 17.1$ Hz); 5.21 (d, 1H, $J = 5.2$ Hz); 5.90 (dd, 1H, $J_1 = 5.2$ Hz, $J_2 = 16.2$ Hz); 6.69-6.81 (m, 3H); 6.96 (d, 1H, $J = 16.2$ Hz); 7.11-7.13 (m, 2H); 7.20-7.25 (m, 2H); 7.34-7.37 (m, 2H). ^{13}C RMN (CDCl_3) δ : 18.5; 22.3; 25.1;

27.3; 31.3; 34.9; 41.4; 47.0; 47.7; 55.2; 56.8; 75.6; 88.4; 110.4; 120.2; 125.6; 125.7; 126.8; 127.0; 127.3 (2C); 127.8 (2C); 128.4; 130.0; 144.1; 156.6. IR (Nujol): 3040, 1595, 1580, 750, 725 cm^{-1} . Anal. Calcd for $\text{C}_{27}\text{H}_{35}\text{NO}_2$: C, 79.96; H, 8.70; N, 3.45. Found: C, 80.09; H, 8.86; N, 3.32.

Reductive Deselenylation of compounds 4d, 4f and 5d. A mixture of AIBN (33 mg, 0.2 mmol), triphenyltin hydride (0.9 g, 2.6 mmol) and toluene (20 mL) was added dropwise via syringe (2 h) to a refluxing solution of **4d**, **4f** or **5d** (2.2 mmol) in 60 mL of toluene under argon atmosphere. The mixture was refluxed for additional 3 h, the solvent was removed in vacuo and the residue was chromatographed on silica gel using hexane/AcOEt, 8/1 as eluent.

(2S,4aS,7R,8aR)-2-[(2S)-2-methoxy-2-(2-methoxy-phenyl)-ethyl]-4,4,7-trimethyl-octahydro-benzo[e][1,3]oxazine (6d). Yield: 80 %. Colorless oil. $[\alpha]_{\text{D}}^{25} = +9.0$ ($c = 1.0$, CHCl_3). ^1H NMR (δ): 0.88-1.11 (m, 4H); 0.92 (d, 3H, $J = 6.5$ Hz); 1.04 (s, 3H); 1.05 (s, 3H); 1.49 (m, 1H); 1.63-1.73 (m, 3H); 1.78 (m, 1H); 1.90-1.99 (m, 2H); 3.20 (s, 3H); 3.37 (td, 1H, $J_1 = 10.5$ Hz, $J_2 = 4.1$ Hz); 3.80 (s, 3H); 4.47 (dd, 1H, $J_1 = 7.3$ Hz, $J_2 = 4.4$ Hz); 4.82 (dd, 1H, $J_1 = 9.0$ Hz, $J_2 = 4.4$ Hz); 6.83 (d, 1H, $J = 8.2$ Hz); 6.95 (t, 1H, $J = 7.5$ Hz); 7.22 (ddd, 1H, $J_1 = 8.2$ Hz, $J_2 = 7.5$ Hz, $J_3 = 1.7$ Hz); 7.35 (dd, 1H, $J_1 = 7.5$ Hz, $J_2 = 1.7$ Hz). ^{13}C RMN (δ): 19.7; 22.2; 25.4; 29.9; 31.3; 34.9; 41.6; 43.1; 51.2; 51.4; 55.2; 56.5; 73.9; 74.8; 80.0; 110.1; 120.5; 127.1; 128.0; 130.2; 157.0. IR (Film): 3300, 3060, 1600, 1585, 795, 755, 670, 620 cm^{-1} . Anal. Calcd for $\text{C}_{21}\text{H}_{33}\text{NO}_3$: C, 72.58; H, 9.57; N, 4.03. Found: C, 72.72; H, 9.69; N, 3.91.

(2S,4aS,7R,8aR)-2-[(2R)-2-methoxy-propyl]-4,4,7-trimethyl-octahydro-benzo[e][1,3]oxazine (6f). Yield: 83 %. Colorless oil. $[\alpha]_{\text{D}}^{25} = -6.5$ ($c = 0.8$, CH_2Cl_2). ^1H NMR (δ): 0.72-1.05 (m, 4H); 0.77 (d, 3H, $J = 6.5$ Hz); 0.91 (s, 3H); 0.92 (s, 3H); 0.98 (d, 3H, $J = 6.2$ Hz); 1.29-1.39 (m, 3H); 1.46-1.62 (m, 3H); 1.78 (m, 1H); 3.17 (s, 3H); 3.24 (td, 1H, $J_1 = 10.3$ Hz, $J_2 = 4.1$ Hz); 3.38 (m, 1H); 4.27 (dd, 1H, $J_1 = 7.7$ Hz, $J_2 = 4.3$ Hz). ^{13}C RMN (δ): 19.0; 19.6; 22.0; 25.2; 29.7; 31.1; 34.7; 41.5; 43.1; 50.9; 51.5; 55.7; 73.0; 74.5; 79.7. IR (Film): 3290, 2925, 1450, 765 cm^{-1} . Anal. Calcd for $\text{C}_{15}\text{H}_{29}\text{NO}_2$: C, 70.54; H, 11.45; N, 5.48. Found: C, 70.39; H, 11.32; N, 5.61.

(2S,4aS,7R,8aR)-2-[(2R)-2-methoxy-2-(2-methoxy-phenyl)-ethyl]-4,4,7-trimethyl-octahydro-benzo[e][1,3]oxazine (7d). Yield: 81 %. Colorless oil. $[\alpha]_{\text{D}}^{25} = +57.0$ ($c = 0.5$, CHCl_3). ^1H NMR (δ): 0.88-1.11 (m, 4H); 0.91 (d, 3H, $J = 6.4$ Hz); 1.04 (s, 3H); 1.09 (s, 3H); 1.46 (m, 1H); 1.64-1.69 (m, 2H); 1.70-2.01 (m, 3H); 2.04 (s,

broad, 1H); 3.22 (s, 3H); 3.35 (dt, 1H, $J_1 = 10.5$ Hz, $J_2 = 4.1$ Hz); 3.81 (s, 3H); 4.43 (dd, 1H, $J_1 = 6.6$ Hz, $J_2 = 4.3$ Hz); 4.86 (dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 4.3$ Hz); 6.85 (d, 1H, $J = 8.1$ Hz); 6.95 (dd, 1H, $J = 8.1$ Hz, $J_2 = 7.5$ Hz); 7.22 (td, 1H, $J_1 = 8.1$ Hz, $J_2 = 1.6$ Hz); 7.36 (dd, 1H, $J_1 = 7.5$ Hz, $J_2 = 1.6$ Hz). ^{13}C RMN (δ): 19.6; 22.3; 25.5; 29.9; 31.4; 35.1; 41.7; 42.5; 51.1; 51.7; 55.3; 56.7; 74.4; 74.9; 80.6; 110.2; 120.6; 126.9; 128.1; 130.2; 160.0. IR (Film): 3330, 1600, 1585, 752 cm^{-1} . Anal. Calcd for $\text{C}_{21}\text{H}_{33}\text{NO}_3$: C, 72.58; H, 9.57; N, 4.03. Found: C, 72.41; H, 9.40; N, 4.16.

Transformation of 4d into 8d. To a suspension of LiAlH_4 (133 mg, 3.5 mmol) in THF (25 mL) cooled to -15 $^\circ\text{C}$ was added, in portions, dry AlCl_3 (156 mg, 1.17 mmol). The mixture was stirred for 10 min, and a solution of **4d** (352 mg, 0.7 mmol) in THF (6 mL) was slowly added. The mixture was stirred 15 min at -15 $^\circ\text{C}$ and quenched by addition of 10% aqueous solution of NaOH (1.0 mL). The resulting mixture was filtered, the solid was washed with EtOAc and the organic layer was dried over anhydrous MgSO_4 . The solvent was eliminated under reduce pressure, and the amino menthol derivative obtained (350 mg, 0.69 mmol) was redissolved in toluene and acetaldehyde (0.12 mL, 2.14 mmol) was added. The mixture was heated in a sealed tube at 80 $^\circ\text{C}$ for 45 hours. The product was purified by flash chromatography on silica gel using a mixture of hexane/EtOAc as eluent to obtain 278 mg (75 % yield) of **8d**. Colorless solid. Mp: 134 – 135 $^\circ\text{C}$ (from EtOH). $[\alpha]_{\text{D}}^{25} = -64.9$ ($c = 1.1$, CH_2Cl_2). ^1H NMR (CDCl_3) δ : 0.74–0.98 (m, 3H); 0.78 (d, 3H, $J = 6.0$ Hz); 0.80 (d, 3H, $J = 6.5$ Hz); 1.06 (m, 1H); 1.08 (s, 3H); 1.27 (s, 3H); 1.31 (m, 1H); 1.49 (m, 1H); 1.57 (m, 1H); 1.68 (m, 1H); 2.95 (d, 2H, $J = 7.8$ Hz); 3.18 (s, 3H); 3.29 (td, 1H, $J_1 = 10.4$ Hz, $J_2 = 4.0$ Hz); 3.57 (s, 3H); 3.73 (td, 1H, $J_1 = 7.8$ Hz, $J_2 = 2.5$ Hz); 4.62 (d, 1H, $J = 2.5$ Hz); 4.67 (q, 1H, $J = 6.0$ Hz); 6.69 (d, 1H, $J = 8.2$ Hz); 6.88 (dd, 1H, $J_1 = 7.5$ Hz, $J_2 = 6.8$ Hz); 7.08–7.21 (m, 4H); 7.28 (dd, 1H, $J_1 = 7.5$ Hz, $J_2 = 1.6$ Hz); 7.60–7.66 (m, 2H). ^{13}C RMN (CDCl_3) δ : 19.6; 21.1; 22.1; 24.7; 28.0; 31.1; 34.8; 39.2; 41.1; 46.0; 53.1; 54.6; 57.0; 57.9; 75.4; 79.1; 82.4; 110.0; 120.3; 126.5 (2C); 127.3; 128.0; 128.2 (2C); 131.9; 134.7 (2C); 156.4. IR (Nujol): 3040, 1595, 1585, 1575, 875, 860, 760, 740, 690 cm^{-1} . Anal. Calcd for $\text{C}_{29}\text{H}_{41}\text{NO}_3\text{Se}$: C, 65.64; H, 7.79; N, 2.64. Found: C, 65.79; H, 7.84; N, 2.59.

Selected structural parameters for **4g** and **4h** in the solid state determined by X-ray crystallographic analysis,

	4g	4h
Interatomic Se...O distance (Å)	2.765	2.773
C(12)-Se(1)-C(13) (deg)	96.500	96.971
C(12)-Se(1)-O(1) (deg)	58.362	58.346
O(1)-Se(1)-C(13) (deg)	154.859	154.810
O(1)-C(1)-C(12)-Se(1) (deg)	16.234	16.566

Ortep representation of X-Ray structure of **4g**

Ortep representation of X-Ray structure of **4h**

Ortep representation of X-Ray structure of **8d**

(333 K)