Supporting Information

for

**Regioselective Synthesis of *N*- β -Hydroxyethylaziridines by the
Ring Opening Reaction of Epoxides with Aziridine
Generated in situ**

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Experimental Section

Chemicals and solvents were reagent grade and used as obtained from commercial sources without further purification. Progress of reactions was monitored by thin layer chromatography (TLC). TLC was performed on glass-backed silica gel 60 F 254 plates (EM reagents, 0.25 mm). TLC plates were visualized with UV (254 nm) and/or with TLC staining solution activated with heat. The commonly employed TLC visualizing solution was *p*-anisaldehyde solution (360 mL absolute ethanol, 20 mL concentrated H₂SO₄, 4 mL glacial acetic acid, 20 mL *p*-anisaldehyde). Analytical samples were obtained from flash column chromatography using 230-400 mesh silica gel. All yields given refer to isolated yields of pure products. Melting points were determined in capillary tubes and are uncorrected. Except where noted, NMR spectra were obtained at 300 MHz (¹H) and 75 MHz (¹³C) using CDCl₃ as solvent and the solvent peak as internal standard. Peak multiplicities in ¹H-NMR spectra are abbreviated as s (singlet), d (doublet), t (triplet), m multiplet, and/or br (broad). Mass spectra were run by the Purdue University campus-wide mass spectrometry facility. The low resolution EI and CI (isobutane) spectra were obtained in a Finnigan 4000 mass spectrometer with a Nova 4 data system with the molecular ion designated as "M⁺". The stock solution of sodium hydroxide was prepared by dissolving 40 g of NaOH in 60 mL of water.

(2S)-1-Aziridin-1-yl-3-benzyloxy-propan-2-ol (entry 1). A solution of 2-chloroethylamine hydrochloride (1.06 g, 9.14 mmol) in water (3.0 mL) and stock NaOH solution (1.10 mL, 18.27 mmol) was heated at 50 °C for 45 min. Benzyl (*S*)-(+)-glycidyl ether (0.50 g, 3.05 mmol) in dioxane (4.0 mL) was added and the reaction mixture was heated at 90 °C. After 12 h the reaction mixture was cooled to room temperature and

diluted with water (10 mL). The resulting solution was extracted with ethyl acetate (3 x 15 mL). The combined organic layer was dried over anhydrous sodium sulfate and evaporated. The crude product was purified by silica gel flash column chromatography (MeOH-EtOAc = 1:9) to give the product (entry 1) as a white solid (0.42 g, 67%): mp 46.5-47.5 °C. IR (film) 3391, 3063, 2859, 1647, 1454, 1091, 739, 699 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.37-7.25 (m, 5 H), 4.55 (s, 2 H), 3.97 (m, 1 H), 3.63-3.47 (m, 2 H), 2.40 (dd, $J = 6.9$ Hz, $J = 12.0$ Hz, 1 H), 2.25 (dd, $J = 4.8$ Hz, $J = 12.0$ Hz, 1 H), 1.78 (t, $J = 5$ Hz, 1 H), 1.74 (t, $J = 5$ Hz, 1 H), 1.23 (dd, $J = 3.9$ Hz, $J = 7.5$ Hz, 1 H), 1.16 (dd, $J = 3.9$ Hz, $J = 7.5$ Hz, 1 H); ^{13}C NMR (CDCl_3) 138.0, 128.3, 127.7, 73.4, 72.5, 69.8, 63.8, 27.5, 26.9; $[\alpha]_{\text{D}}^{23} = -11.9$ (c 1, CHCl_3); EIMS m/z (rel intensity) 116 ($\text{M}^+ - \text{C}_7\text{H}_7$, 30), 91 (C_7H_7^+ , 55), 56 ($\text{C}_3\text{H}_6\text{N}^+$, 100); CIMS m/z (rel intensity) 208 (MH^+ , 100). Anal. Calcd for $\text{C}_{12}\text{H}_{17}\text{NO}_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.58; H, 8.25; N, 6.78.

2-(Aziridin-1-yl)-1-(4-chlorophenyl)ethanol (entry 2). A solution of 2-chloroethylamine hydrochloride (0.75 g, 6.47 mmol) in water (3.2 mL) and stock NaOH solution (0.78 mL, 12.94 mmol) was heated at 50 °C for 45 min. 2-(4-chlorophenyl)oxirane (0.50 g, 3.23 mmol) in dioxane (4.0 mL) was added and the reaction mixture was heated at 90 °C. After 12 h the reaction mixture was cooled to room temperature and diluted with water (10 mL). The resulting solution was extracted with ethyl acetate (3 x 15 mL). The combined organic layer was dried over anhydrous sodium sulfate and evaporated. The crude product was purified by silica gel flash column chromatography (MeOH-EtOAc = 1:9) to afford the product (entry 2) as a clear oil (0.53 g, 83%): IR (film) 3350, 3066, 2991, 2834, 1648, 1491, 1266, 1090, 1014, 822 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.31-7.24 (m, 4 H), 4.78 (dd, $J = 3.6$ Hz, $J = 8.9$ Hz, 1 H), 3.79 (d, $J =$

5.3 Hz, 1 H), 2.65 (dd, $J = 8.9$ Hz, $J = 12.0$ Hz, 1 H), 2.10 (dd, $J = 3.6$ Hz, $J = 12.0$ Hz, 1 H), 1.81-1.67 (m, 2 H), 1.26-1.14 (m, 2 H); ^{13}C NMR (CDCl_3) 140.6, 128.9, 128.5, 127.3, 75.1, 72.4, 68.9, 67.3, 27.6, 27.0; EIMS m/z (rel intensity) 168 ($\text{M}^+ - \text{C}_2\text{H}_4\text{N} + 1$, 9), 166 ($\text{M}^+ - \text{C}_2\text{H}_4\text{N} - 1$, 24), 56 ($\text{C}_3\text{H}_6\text{N}^+$, 100); CIMS m/z (rel intensity) 200 ($\text{MH}^+ + 2$, 28), 198 (MH^+ , 87), 182 ($\text{MH}^+ - \text{H}_2\text{O} + 2$, 34), 180 ($\text{MH}^+ - \text{H}_2\text{O}$, 100). Anal. Calcd for $\text{C}_{10}\text{H}_{12}\text{ClNO}$: C, 60.76; H, 6.12; N, 7.09; Cl, 17.94. Found: C, 60.66; H, 6.13; N, 7.08; Cl, 17.90.

2-(Aziridin-1-yl)-1-phenylethanol (entry 3). A solution of 2-chloroethylamine hydrochloride (0.97 g, 8.32 mmol) in water (3.0 mL) and stock NaOH solution (1.0 mL, 16.65 mmol) at was heated at 50 °C for 45 min. Styrene oxide (0.50 g, 4.16 mmol) in dioxane (4.0 mL) was added and the reaction mixture was heated at 90 °C. After 12 h the reaction mixture was cooled to room temperature and diluted with water (10 mL). The resulting solution was extracted with ethyl acetate (3 x 15 mL). The combined organic layer was dried over anhydrous sodium sulfate and evaporated. The crude product was purified by silica gel flash column chromatography (MeOH-EtOAc = 1:9) to yield the product (entry 3) as a clear oil (0.44 g, 65%): IR (film) 3351, 3062, 2833, 1646, 1493, 1452, 1265, 1067, 758, 701 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.39-7.21 (m, 5 H), 4.82 (dd, $J = 3.5$ Hz, $J = 9.0$ Hz, 1 H), 3.85 (m, 1 H), 2.72 (dd, $J = 9.0$ Hz, $J = 12.0$ Hz, 1 H), 2.13 (dd, $J = 3.5$ Hz, $J = 12.0$ Hz, 1 H), 1.85-1.68 (m, 2 H), 1.24 (m, 1 H), 1.16 (m, 1 H); ^{13}C NMR (CDCl_3) 142.1, 128.3, 127.6, 125.9, 73.2, 69.1, 27.6, 27.0; EIMS m/z (rel intensity) 162 ($\text{M}^+ - 1$, 1), 132 ($\text{M}^+ - 31$, 56), 56 ($\text{C}_3\text{H}_6\text{N}^+$, 100); CIMS m/z (rel intensity) 164 (MH^+ , 34), 146 ($\text{MH}^+ - \text{H}_2\text{O}$, 100). Anal. Calcd for $\text{C}_{10}\text{H}_{13}\text{NO}$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.49; H, 8.05; N, 8.60.

2-(Aziridin-1-yl)-1-cyclopentanol (entry 4). A solution of 2-chloroethylamine hydrochloride (1.38 g, 11.89 mmol) in water (2.6 mL) and stock NaOH solution (1.43 mL, 23.78 mmol) at was heated at 50 °C for 45 min. Cyclopentene oxide (0.50 g, 5.94 mmol) in dioxane (4.0 mL) was added and the reaction mixture was heated at 90 °C. After 12 h the reaction mixture was cooled to room temperature and diluted with water (10 mL). The resulting solution was extracted with ethyl acetate (3 x 15 mL). The combined organic layer was dried over anhydrous sodium sulfate and evaporated. The crude product was purified by silica gel flash column chromatography (MeOH-EtOAc = 1:9) to provide the product (entry 4) as a clear oil (0.45 g, 60%): IR (film) 3350, 2958, 1451, 1359 cm^{-1} ; ^1H NMR (CDCl_3) δ 4.13 (m, 1 H), 2.29 (brs, 1 H), 2.07 (m, 1 H), 1.86 (m, 1 H), 1.68-1.62 (m, 6 H), 1.54 (m, 1 H), 1.36 (dd, $J = 4.0$ Hz, $J = 7.1$ Hz, 1 H), 1.12 (dd, $J = 4.0$ Hz, $J = 7.1$ Hz, 1 H); ^{13}C NMR (CDCl_3) 77.4, 76.5, 32.8, 28.9, 25.9, 24.7. 20.3; EIMS m/z (rel intensity) 126 ($\text{M}^+ - 1$, 4), 44 ($\text{M}^+ - 123$, 100); CIMS m/z (rel intensity) 128 (MH^+ , 79), 110 ($\text{MH}^+ - \text{H}_2\text{O}$, 100). Anal. Calcd for $\text{C}_7\text{H}_{13}\text{NO}$: C, 66.10; H, 10.30; N, 11.01. Found: C, 66.29; H, 10.25; N, 10.98.

2-(Aziridin-1-yl)-1-cyclohexanol (entry 5). A solution of 2-chloroethylamine hydrochloride (1.18 g, 10.18 mmol) in water (2.8 mL) and stock NaOH solution (1.22 mL, 20.36 mmol) was heated at 50 °C for 45 min. Cyclohexene oxide (0.50 g, 5.09 mmol) in dioxane (4.0 mL) was added and the reaction mixture was heated at 90 °C. After 12 h the reaction mixture was cooled to room temperature and diluted with water (10 mL). The resulting solution was extracted with ethyl acetate (3 x 15 mL). The combined organic layer was dried over anhydrous sodium sulfate and evaporated. The

crude product was purified by silica gel flash column chromatography (MeOH-EtOAc = 1:9) to yield the product (entry 5) as a white solid (0.42 g, 58%): mp 208-210 °C. IR (film) 3409, 2930, 2857, 1450, 1355, 1266 cm^{-1} ; ^1H NMR (CDCl_3) δ 3.61 (m, 1 H), 2.63 (brs, 1 H), 1.91 (m, 1 H), 1.85 (dd, $J = 4.2$ Hz, $J = 5.8$ Hz, 1 H), 1.78 (m, 1 H), 1.66 (m, 2 H), 1.60 (dd, $J = 4.1$ Hz, $J = 5.8$ Hz, 1 H), 1.52 (dd, $J = 4.1$ Hz, $J = 7.2$ Hz, 1 H), 1.23 (m, 3 H), 1.16 (m, 1 H), 1.07 (m, 2 H); ^{13}C NMR (CDCl_3) 74.1, 73.8, 33.6, 30.3, 28.6, 24.1, 24.0, 22.3; EIMS m/z (rel intensity) 141 (M^+ , 13), 82 ($\text{M}^+ - 59$, 61), 44 ($\text{M}^+ - 97$, 100); CIMS m/z (rel intensity) 142 (MH^+ , 100), 124 ($\text{MH}^+ - \text{H}_2\text{O}$, 36). Anal. Calcd for $\text{C}_8\text{H}_{15}\text{NO}$: C, 68.04; H, 10.71; N, 9.92. Found: C, 68.29; H, 10.67; N, 9.89.

(*1R,2R*)-2-(Aziridin-1-yl)-1,2-diphenylethanol (entry 6). A solution of 2-chloroethylamine hydrochloride (0.30 g, 2.55 mmol) in water (1.7 mL) and stock NaOH solution (0.31 mL, 5.09 mmol) was heated at 50 °C for 45 min. *trans*-Stilbene oxide (0.25 g, 1.27 mmol) in dioxane (2.0 mL) was added and the reaction mixture was heated at 90 °C. After 12 h the reaction mixture was cooled to room temperature and diluted with water (10 mL). The resulting solution was extracted with ethyl acetate (3 x 15 mL). The combined organic layer was dried over anhydrous sodium sulfate and evaporated. The crude product was purified by silica gel flash column chromatography (MeOH-EtOAc = 0.5:9.5) to afford the product (entry 6) as a white solid (0.20 g, 65%): mp 137-139 °C. IR (film) 3400, 3062, 2840, 1494, 1452, 1261 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.28 (m, 10 H), 5.05 (d, $J = 5.7$ Hz, 1 H), 2.89 (brs, 1 H), 2.50 (d, $J = 5.7$ Hz, 1 H), 1.71 (m, 2 H), 1.14 (m, 2 H); ^{13}C NMR (CDCl_3) 141.3, 139.1, 128.6, 127.8, 127.5, 127.4, 126.8, 81.2, 77.1, 30.0, 25.8; EIMS m/z (rel intensity) 132 ($\text{M}^+ - \text{C}_6\text{H}_5\text{CHOH}$, 100); CIMS m/z (rel intensity) 240

(MH⁺, 31), 222 (MH⁺ - H₂O, 22), 107 (M⁺ - C₆H₅CHOH, 100). Anal. Calcd for C₁₆H₁₇NO: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.50; H, 7.13; N, 5.83.

1-(Aziridin-1-yl)-hexanol (entry 7). A solution of 2-chloroethylamine hydrochloride (9.98 g, 1.16 mmol) in water (2.8 mL) and stock NaOH solution (1.20 mL, 19.96 mmol) was heated at 45 °C for 45 min. 1,2-Epoxyhexane (0.50 g, 4.99 mmol) in dioxane (4.0 mL) was added and the reaction mixture was heated at 90 °C. After 12 h the reaction mixture was cooled to room temperature and diluted with water (10 mL). The resulting solution was extracted with ethyl acetate (3 x 15 mL). The combined organic layer was dried over anhydrous sodium sulfate and evaporated. The crude product was purified by silica gel flash column chromatography (MeOH-EtOAc = 0.5:9.5) to give the product (entry 7) as a clear oil (0.48 g, 67%): IR (film) 3392, 3060, 2956, 2931, 2860, 1467, 1268, 1003 cm⁻¹; ¹H NMR (CDCl₃) δ 3.66 (m, 1 H), 3.55 (m, 1 H), 2.39 (dd, *J* = 8.6 Hz, *J* = 11.9 Hz, 1 H), 1.92 (dd, *J* = 3.2 Hz, *J* = 11.9 Hz, 1 H), 1.75 (dd, *J* = 4.0 Hz, *J* = 5.9 Hz, 1 H), 1.68 (dd, *J* = 4.0 Hz, *J* = 5.9 Hz, 1 H), 1.41-1.19 (m, 7 H), 1.07 (dd, *J* = 4.0 Hz, *J* = 7.0 Hz, 1 H), 0.84 (t, *J* = 6.7 Hz, 3 H); ¹³C NMR (CDCl₃) 70.3, 67.6, 34.5, 27.6, 27.5, 26.5, 22.5, 13.8; EIMS *m/z* (rel intensity) 142 (M⁺ - 1, 2), 56 (M⁺ - 87, 100), 44 (M⁺ - 99, 27); CIMS *m/z* (rel intensity) 144 (MH⁺, 100), 126 (MH⁺ - H₂O, 55). Anal. Calcd for C₈H₁₅NO: C, 68.04; H, 10.71; N, 9.99. Found: C, 73.49; H, 8.05; N, 8.60.

1-(Aziridin-1-yl)-hex-5-en-2-ol (entry 8). A solution of 2-chloroethylamine hydrochloride (0.59 g, 5.09 mmol) in water (1.4 mL) and stock NaOH solution (0.61 mL, 10.19 mmol) was heated at 50 °C for 45 min. 1,2-Epoxy-5-hexene (0.25 g, 2.55 mmol) in dioxane (2.0 mL) was added and the reaction mixture was heated at 90 °C. After 12 h the reaction mixture was cooled to room temperature and diluted with water (10 mL). The

resulting solution was extracted with ethyl acetate (3 x 15 mL). The combined organic layer was dried over anhydrous sodium sulfate and evaporated. The crude product was purified by silica gel flash column chromatography (MeOH-EtOAc = 0.5:9.5) to provide the product (entry 8) as a clear oil (0.22 g, 61%): IR (film) 3402, 3076, 2936, 1641, 1448, 1301 cm^{-1} ; ^1H NMR (CDCl_3) δ 5.76 (m, 1 H), 4.94 (d, $J = 17.1$ Hz, 1 H), 4.88 (d, $J = 10.7$ Hz, 1 H), 3.88 (brs, 1 H), 3.63 (m, 1 H), 2.35 (dd, $J = 8.6, 11.7$, 1 H), 2.22-1.91 (m, 2 H), 1.93 (dd, $J = 3.2, 11.7$ Hz, 1 H), 1.74 (m, 1 H), 1.64 (m, 1 H), 1.51-1.34 (m, 2 H), 1.19 (dd, $J = 3.9, 7.0$ Hz, 1 H), 1.06 (dd, $J = 3.9, 7.0$ Hz, 1 H); ^{13}C NMR (CDCl_3) 138.1, 114.2, 69.4, 67.4, 33.8, 29.6, 27.4, 26.4; EIMS m/z (rel intensity) 141 (M^+ , 0.3), 56 ($\text{M}^+ - 85$, 100), 44 ($\text{M}^+ - 97$, 24); CIMS m/z (rel intensity) 142 (MH^+ , 100), 124 ($\text{MH}^+ - \text{H}_2\text{O}$, 26). Anal. Calcd for $\text{C}_8\text{H}_{17}\text{NO}$: C, 67.09; H, 10.96; N, 9.78. Found: C, 67.12; H, 10.99; N, 9.80.

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Vial Number : 1
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Vial Number: 1

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Misc Info : DIP
Vial Number: 1

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Operator : A.R.
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Sample Name: DIPHEN-AZIDINE
Misc Info : DIP
Vial Number: 1

CI

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 Vial Number: 1

Current Data Parameters
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C13CPD256

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