

The First Transformation of Aliphatic α,β -Epoxyamides into α -Hydroxyamides.

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SUPPORTING INFORMATION

SPECTROSCOPIC DATA OF COMPOUNDS 1

General Procedure for the Synthesis of 2,3-Epoxyamide 1a:
Disubstituted epoxyamide, compound **1a** was prepared from Sharpless epoxidation of the corresponding allyl alcohol,¹⁶ further oxidation¹⁷ and conversion into the amide.¹⁸

(2S,3R)-2,3-Epoxy-N-methyldecanamide (1a)

¹H NMR (200 MHz, CDCl₃): δ = 6.30 (br, NH), 3.14 (d, J = 2.1 Hz, 1 H), 2.90-2.84 (m, 1 H), 2.72 (d, J = 5.1 Hz, 3 H), 1.68-0.95 (m, 12 H), 0.80 (t, J = 6.7 Hz, 3 H); ¹³C NMR (50 MHz, CDCl₃): δ = 169.1 (C), 59.4 (CH), 55.1 (CH), 30.7 (CH₂), 28.9 (CH₂), 28.8 (CH₂), 25.4 (CH₂), 25.2 (CH₂), 22.3 (CH₃), 13.1 (CH₃); IR (neat): $\tilde{\nu}$ = 3275, 1663, 1461, 1280 cm⁻¹; R_f = 0.1 (hexane/AcOEt 1/1); $[\alpha]^{25}_D$ = +15.7 (c = 0.09 in CHCl₃).

General Procedure for the Synthesis of 2,3-Epoxyamides 1b-c:

To a -78 °C stirred solution of the corresponding 2-chloroamide (4.5 mmol) in dry THF (4 mL) was added dropwise lithium diisopropylamide [prepared from MeLi (3.2 mL of 1.5 M

solution in diethyl ether, 5 mmol) and diisopropylamine (0.8 ml, 5 mmol) in THF 25 mL at 0 °C]. After stirring for 10 min, a solution of the corresponding aldehyde (3.5 mmol) in dry THF (4.5 mL) was added dropwise at -78 °C and the mixture was stirred for 1 h. Then, the reaction mixture was quenched with aqueous saturated solution of NH₄Cl (20 mL) and usual workup provided crude 2-halo-3-hydroxyamides, which were diluted with CH₂Cl₂ (20 mL) and treated with sodium hydride (1g, 45 mmol) at 25°C. The mixture was stirred for 2.5 hours at this temperature. Then quenched with H₂O and extracted with CH₂Cl₂ (3 x 10 mL). The combined organic layers were dried (Na₂SO₄), filtered, and concentrated in vacuo. The crude 2,3-epoxyamides **1b-d** were purified by flash column chromatography on silica gel (hexane/AcOEt) to provide pure compounds.

2,3-Epoxy-*N,N*-diethyldecanamide (1b)

¹H NMR (300 MHz, CDCl₃): δ = 3.51 (d, *J* = 4.4 Hz, 1 H), 3.49-3.05 (m, 11 H), 1.63-1.14 (m, 30 H), 1.19-0.98 (m, 6 H), 0.82-0.69 (m, 6 H); ¹³C NMR (75 MHz, CDCl₃): δ = 166.4 (C), 165.5 (C), 57.8 (CH), 56.8 (CH), 53.7 (CH), 53.1 (CH), 41.1 (CH₂), 40.7 (CH₂), 40.4 (CH₂), 39.7 (CH₂), 31.4 (CH₂), 29.0 (CH₂), 28.9 (CH₂), 28.8 (CH₂), 27.9 (CH₂), 25.9 (CH₂), 25.6 (CH₂), 22.2 (CH₂), 14.5 (CH₃), 14.0 (CH₃), 13.7 (CH₃), 12.6

(CH₃); IR (neat): $\tilde{\nu}$ = 2929, 1657, 1468, 1265 cm⁻¹; R_f = 0.1 (hexane/AcOEt 3/1).

3-Cyclohexyl-2,3-epoxy-*N,N*-diisopropylpropanamide (1c)

¹H NMR (200 MHz, CDCl₃): δ = 4.34-4.21 (m, 1 H), 3.53 (d, *J* = 4.4 Hz, 1 H), 3.53-3.37 (m, 1 H), 2.93-2.86 (m, 1 H), 2.06-1.57 (m, 11 H), 1.42 (d, *J* = 6.7 Hz, 6 H), 1.25 (d, *J* = 6.7 Hz, 3 H), 1.23 (d, *J* = 6.7 Hz, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ = 164.2 (C), 60.0 (CH), 53.5 (CH), 46.6 (CH), 44.6 (CH), 35.5 (CH), 29.1 (CH₂), 27.5 (CH₂), 25.0 (CH₂), 24.2 (CH₂), 24.1 (CH₂), 19.7 (CH₃), 19.4 (CH₃), 19.1 (CH₃), 18.8 (CH₃); IR (neat): $\tilde{\nu}$ = 2953, 1651, 1454, 1372, 1136 cm⁻¹; R_f = 0.2 (hexane/AcOEt 3/1).

2,3-Epoxy-*N,N*-diethyl-5,9-dimethyldecanamide (1d)

¹H NMR (200 MHz, CDCl₃): δ = 5.05-4.88 (m, 2 H), 4.00-3.97 (m, 2 H), 3.54-2.99 (m, 10 H), 2.01-0.82 (m, 32 H), 1.55 (s, 6 H), 1.47 (s, 6 H); ¹³C NMR (50 MHz, CDCl₃): δ = 166.3 (C), 165.4 (C), 130.8 (C), 124.1 (CH), 124.0 (CH), 55.7 (CH), 55.5 (CH), 53.4 (CH), 53.0 (CH), 40.6 (CH₂), 39.6 (CH₂), 36.6 (CH₂), 34.7 (CH₂), 30.7 (CH), 30.2 (CH), 25.3 (CH₃), 25.0 (CH₂), 19.3 (CH₃), 19.0 (CH₃), 17.2 (CH₃), 14.5 (CH₃), 13.9 (CH₃), 12.5 (CH₃), 12.2 (CH₃); IR (neat): $\tilde{\nu}$ = 2973, 1649, 1463, 1381, 1147 cm⁻¹; R_f = 0.4 (hexane/AcOEt 1/1).

General Procedure for the Synthesis of 2,3-Epoxyamides 1e-i: To a -78 °C stirred solution of the corresponding 2-chloroamide (2.5 mmol) in dry THF (4 mL) was added dropwise potassium hexamethyldisilazide (6.5 mL of 0.5 M solution in toluene, 3.25 mmol). After stirring for 10 min, a solution of the corresponding aldehyde (2.5 mmol) in dry THF (4 mL) was added dropwise at -78 °C and the mixture was allowed to warm to room temperature. The resulting solution was quenched with aqueous saturated solution of NH₄Cl (20 mL). The usual workup provided crude 2,3-epoxyamides **1e-i**, which were purified by column flash chromatography over silica gel (hexane/ethyl acetate) provided pure compound.

2,3-Epoxy-*N,N*-diethyl-2,5-dimethylhexanamide (1e)

¹H NMR (200 MHz, CDCl₃): δ = 3.59-3.12 (m, 8 H), 3.02-2.96 (m, 2 H), 1.87-1.24 (m, 6 H), 1.43 (s, 6 H), 1.15 (t, *J* = 7.1 Hz, 6 H), 1.07 (t, *J* = 7.1 Hz, 6 H), 0.96 (d, *J* = 6.7 Hz, 12 H); ¹³C NMR (75 MHz, CDCl₃): δ = 170.0 (C), 62.7 (C), 61.0 (CH), 60.6 (C), 41.0 (CH₂), 39.1 (CH₂), 36.5 (CH), 26.4 (CH₂), 22.6 (CH₃), 22.2 (CH₃), 15.6 (CH₃), 14.0 (CH₃), 12.4 (CH₃); IR (neat): $\tilde{\nu}$ = 2959, 1639, 1467, 1382, 1073 cm⁻¹; *R_f* = 0.2 (hexane/AcOEt 3/1).

2,3-Epoxy-*N,N*-diethyl-2-methyldecanamide (1f)

^1H NMR (200 MHz, CDCl_3): δ = 3.56-2.96 (m, 10 H), 1.50 (s, 3 H), 1.45 (s, 3 H), 1.42-1.20 (m, 24 H), 1.15 (t, J = 7.1 Hz, 6 H), 1.08 (t, J = 7.1 Hz, 6 H), 0.89-0.79 (m, 6 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 169.9 (C), 168.5 (C), 63.9 (C), 61.9 (C), 61.2 (CH), 60.8 (CH), 41.3 (CH_2), 41.0 (CH_2), 39.2 (CH_2), 39.1 (CH_2), 31.5 (CH_2), 30.0 (CH_2), 29.1 (CH_2), 29.0 (CH_2), 27.8 (CH_2), 26.1 (CH_2), 22.4 (CH_2), 20.5 (CH_2), 15.4 (CH_3), 14.1 (CH_3), 14.0 (CH_3), 13.9 (CH_3), 12.4 (CH_3), 12.3 (CH_3); IR (neat): $\tilde{\nu}$ = 2927, 1644, 1464, 1380, 1079 cm^{-1} ; R_f = 0.1 (hexane/AcOEt 5/1).

3-Cyclohexyl-2,3-epoxy-*N,N*-diethyl-2-methylpropanamide (1g)

^1H NMR (200 MHz, CDCl_3): δ = 3.69-3.20 (m, 8 H), 2.75 (d, J = 7.4 Hz, 1 H), 2.57 (d, J = 8.2 Hz, 1 H), 2.01-1.39 (m, 22 H), 1.53 (s, 3 H), 1.51 (s, 3 H), 1.19 (t, J = 6.9 Hz, 6 H), 1.11 (t, J = 6.9 Hz, 6 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 169.8 (C), 67.6 (C), 65.8 (C), 61.8 (CH), 60.9 (CH), 41.6 (CH_2), 40.9 (CH_2), 39.0 (CH_2), 38.6 (CH_2), 36.8 (CH), 30.0 (CH_2), 29.8 (CH_2), 28.3 (CH_2), 28.2 (CH_2), 26.0 (CH_2), 25.9 (CH_2), 25.2 (CH_2), 25.1 (CH_2), 15.5 (CH_3), 14.2 (CH_3), 14.0 (CH_3), 12.4 (CH_3), 12.3 (CH_3); IR (neat): $\tilde{\nu}$ = 2930, 1636, 1450, 1381, 1074 cm^{-1} ; R_f = 0.2, 0.3 (hexane/AcOEt 3/1).

2-Butyl-3-cyclohexyl-2,3-epoxy-*N,N*-diethylpropanamide (1h)

^1H NMR (200 MHz, CDCl_3): δ = 3.61-3.68 (m, 4 H), 2.16 (d, J = 6.4 Hz, 1 H), 2.02-1.03 (m, 23 H), 0.86 (t, J = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 169.2 (C), 66.2 (CH), 64.1 (C), 40.9 (CH_2), 39.2 (CH_2), 36.5 (CH), 30.2 (CH_2), 29.7 (CH_2), 28.6 (CH_2), 27.2 (CH_2), 25.9 (CH_2), 25.2 (CH_2), 22.8 (CH_2), 14.1 (CH_3), 13.7 (CH_3), 12.4 (CH_3); IR (neat): $\tilde{\nu}$ = 2960, 1644, 1460, 1381, 1131 cm^{-1} ; R_f = 0.3 (hexane/AcOEt 3/1).

2,3-Epoxy-*N,N*-diethyl-2,5,9-trimethyldecan-8-enamide (1i)

^1H NMR (200 MHz, CDCl_3): δ = 5.13-5.05 (m, 2 H), 3.68-3.03 (m, 10 H), 2.10-1.31 (m, 14 H), 1.68 (s, 6 H), 1.60 (s, 6 H), 1.49 (s, 6 H), 1.20 (t, J = 7.1 Hz, 6 H), 1.15 (t, J = 7.2 Hz, 6 H), 1.01 (d, J = 6.4 Hz, 6 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 169.7 (C), 168.2 (C), 130.6 (C), 124.1 (CH), 124.0 (CH), 60.7 (CH), 60.6 (CH), 59.9 (C), 41.1 (CH_2), 40.7 (CH_2), 39.1 (CH_2), 38.8 (CH_2), 36.6 (CH_2), 36.4 (CH_2), 34.5 (CH_2), 34.4 (CH_2), 30.6 (CH), 30.2 (CH), 25.2 (CH_2), 24.9 (CH_3), 20.1 (CH_3), 19.2 (CH_3), 18.8 (CH_3), 17.1 (CH_3), 15.3 (CH_3), 15.2 (CH_3), 13.7 (CH_3), 12.0 (CH_3); IR (neat): $\tilde{\nu}$ = 2968, 1644, 1635, 1434, 1380, 1076 cm^{-1} ; R_f = 0.3 (hexane/AcOEt 5/1).

SPECTROSCOPIC DATA OF COMPOUNDS 2

(2S)-2-Hydroxy-*N*-methyldecanamide (2a)

^1H NMR (200 MHz, CDCl_3): δ = 6.57 (br, NH), 4.21-4.05 (m, 1 H), 2.86 (d, J = 3.6, 3 H), 1.99-1.17 (m, 14 H), 0.88 (t, J = 6.4, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 174.5 (C), 72.2 (CH), 34.9 (CH_2), 31.8 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 25.7 (CH_3), 25.0 (CH_2), 22.6 (CH_2), 14.0 (CH_3); MS (70 eV): m/z (%): 201 $[M]^+$ (4), 102 (25), 88 (37), 58 (85); IR (neat): $\tilde{\nu}$ = 3054, 1668 cm^{-1} ; R_f = 0.1 (hexane/AcOEt 1/1); $[\alpha]^{25}_{\text{D}}$ = +24.0 (c = 0.05 in CHCl_3).

***N,N*-Diethyl-2-hydroxydecanamide (2b)**

¹H NMR (400 MHz, DMSO): δ = 4.21 (dd, J = 7.1, 4.7 Hz, 1 H), 3.87-3.26 (m, 4 H), 1.72-1.34 (m, 14 H), 1.32 (t, J = 7.1, 3 H), 1.25 (t, J = 7.1, 3 H), 0.98 (t, J = 7.1, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ = 173.6 (C), 67.8 (CH), 40.7 (CH₂), 40.0 (CH₂), 35.3 (CH₂), 31.7 (CH₂), 29.3 (CH₂), 29.0 (CH₂), 24.8 (CH₂), 22.5 (CH₂), 13.9 (CH₃), 12.6 (CH₃); MS (70 eV): m/z (%): 243 [M]⁺ (3), 226 (2), 130 (43), 100 (100); HRMS calcd for C₁₄H₂₉NO₂ 243.2198, found 243.2185; IR (neat): $\tilde{\nu}$ = 3418, 1638 cm⁻¹; R_f = 0.2 (hexane/AcOEt 3/1).

3-Cyclohexyl-2-hydroxy-*N,N*-Diisopropyldecanamide (2c)

¹H NMR (400 MHz, DMSO): δ = 4.32-3.35 (m, 6 H), 1.77-0.86 (m, 11 H), 1.26 (d, J = 6.9, 6 H), 1.25 (d, J = 6.9, 6 H),; ¹³C NMR (75 MHz, CDCl₃): δ = 173.5 (C), 66.1 (CH), 47.4 (CH), 45.9 (CH), 43.2 (CH₂), 34.3 (CH₂), 33.8 (CH), 32.1 (CH₂), 26.3 (CH₂), 26.1 (CH₂), 25.8 (CH₂), 20.7 (CH₃), 20.4 (CH₃), 19.3 (CH₃); MS (70 eV): m/z (%): 255 [M]⁺ (<1), 212 (5), 158 (11), 128 (65), 83 (25); HRMS calcd for C₁₅H₂₉NO₂ 255.2198, found 255.2189; IR (neat): $\tilde{\nu}$ = 3365, 1702 cm⁻¹; R_f = 0.4 (hexane/AcOEt 3/1).

***N,N*-Diethyl-2-hydroxy-5,9-dimethyldecan-8-enamide (2d)**

¹H NMR (300 MHz, DMSO): δ = 5.09-4.98 (m, 4 H), 4.26-4.08 (m, 4 H), 3.33-3.15 (m, 8 H), 1.97-0.92 (m, 36 H), 1.58 (s, 12

H), 1.51 (s, 12 H), 1.02 (t, $J = 7.1$ Hz, 24 H), 0.83-0.74 (m, 12 H); ^{13}C NMR (75 MHz, CDCl_3): $\delta = 173.6$ (C), 130.9 (C), 124.6 (CH), 68.2 (CH), 68.1 (CH), 40.7 (CH_2), 40.0 (CH_2), 37.0 (CH_2), 36.5 (CH_2), 32.8 (CH_2), 32.1 (CH), 31.9 (CH_2), 31.8 (CH_2), 25.5 (CH_3), 25.4 (CH_2), 25.3 (CH_2), 19.5 (CH_3), 19.2 (CH_3), 17.5 (CH_3), 13.0 (CH_3), 12.7 (CH_3); MS (70 eV): m/z (%): 269 $[M]^+$ (29), 200 (100), 130 (32), 100 (100), 69 (54); IR (neat): $\tilde{\nu} = 3417, 1640\text{ cm}^{-1}$; $R_f = 0.3$ (hexane/AcOEt 5/1).

***N,N*-Diethyl-2-hydroxy-2,5-dimethylhexanamide (2e)**

^1H NMR (300 MHz, DMSO): $\delta = 4.75$ (br, 1 H), 3.49-3.28 (m, 4 H), 1.74-1.11 (m, 5 H), 1.31 (s, 3 H), 1.08 (t, $J = 6.6$, 6 H), 0.85 (d, $J = 6.4$, 6 H); ^{13}C NMR (50 MHz, CDCl_3): $\delta = 174.9$ (C), 73.6 (C), 42.0 (CH_2), 41.5 (CH_2), 38.3 (CH_2), 32.4 (CH_2), 28.1 (CH), 26.6 (CH_3), 22.5 (CH_3), 13.9 (CH_3), 12.4 (CH_3); MS (70 eV): m/z (%): 215 $[M]^+$ (<1), 144 (23), 100 (35), 71 (16), 43 (100); IR (neat): $\tilde{\nu} = 3385, 1613\text{ cm}^{-1}$; $R_f = 0.3$ (hexane/AcOEt 3/1).

***N,N*-Diethyl-2-hydroxy-2-methyldecanamide (2f)**

^1H NMR (300 MHz, DMSO): $\delta = 3.53$ -3.40 (m, 4 H), 1.80-1.22 (m, 14 H), 1.34 (s, 3 H), 1.11 (t, $J = 7.0$, 6 H), 0.88 (t, $J = 6.7$, 3 H); ^{13}C NMR (75 MHz, CDCl_3): $\delta = 174.9$ (C), 73.6 (C), 42.1 (CH_2), 41.5 (CH_2), 40.5 (CH_2), 31.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 26.5 (CH_3), 23.5 (CH_2), 22.5 (CH_2),

14.0 (CH₃), 13.9 (CH₃), 12.4 (CH₃); MS (70 eV): *m/z* (%): 257 [*M*]⁺ (<1), 157 (95), 144 (87), 72 (86), 43 (83); HRMS calcd for C₁₅H₃₁NO₂ 257.2355, found 257.2361; IR (neat): $\tilde{\nu}$ = 3388, 1622 cm⁻¹; R_f = 0.3 (hexane/AcOEt 3/1).

3-Cyclohexyl-*N,N*-diethyl-2-hydroxy-2-methylpropanamide (2g)

¹H NMR (300 MHz, DMSO): δ = 3.57-3.40 (m, 4 H), 1.76-0.87 (m, 13 H), 1.38 (s, 3 H), 1.13 (t, *J* = 7.0, 6 H); ¹³C NMR (75 MHz, CDCl₃): δ = 175.3 (C), 73.4 (C), 47.7 (CH₂), 42.1 (CH₂), 41.3 (CH₂), 34.5 (CH₂), 33.9 (CH₂), 33.6 (CH), 27.5 (CH₃), 26.1 (CH₂), 26.0 (CH₂), 13.7 (CH₃), 12.0 (CH₃); MS (70 eV): *m/z* (%): 241 [*M*]⁺ (<1), 100 (62), 97 (13), 83 (73), 72 (95); IR (neat): $\tilde{\nu}$ = 3383, 1614 cm⁻¹; R_f = 0.3 (hexane/AcOEt 3/1).

2-Butyl-3-cyclohexyl-*N,N*-diethyl-2-hydroxypropanamide (2h)

¹H NMR (300 MHz, DMSO): δ = 3.49-3.42 (m, 4 H), 1.79-0.91 (m, 19 H), 1.22 (t, *J* = 6.9, 6 H), 0.86 (t, *J* = 7.3, 3 H); ¹³C NMR (50 MHz, CDCl₃): δ = 174.6 (C), 76.6 (C), 47.3 (CH₂), 42.1 (CH₂), 41.3 (CH₂), 40.3 (CH₂), 34.6 (CH₂), 34.2 (CH₂), 33.7 (CH), 26.2 (CH₂), 25.4 (CH₂), 22.8 (CH₂), 22.5 (CH₂), 13.9 (CH₃), 13.5 (CH₃), 12.1 (CH₃); MS (70 eV): *m/z* (%): 283 [*M*]⁺ (<1), 186 (18), 183 (100), 97 (66), 83 (95); HRMS calcd for C₁₇H₃₃NO₂ 283.2511, found 283.2505 ;IR (neat): $\tilde{\nu}$ = 3375, 1625 cm⁻¹; R_f = 0.3 (hexane/AcOEt 3/1)

***N,N*-Diethyl-2-hydroxy-2,5,9-trimethyldec-8-enamide (2i).**

^1H NMR (300 MHz, DMSO): δ = 5.14-5.08 (m, 2 H), 3.54-3.41 (m, 8 H), 2.02-0.98 (m, 18 H), 1.66 (s, 3 H), 1.59 (s, 3 H), 1.34 (s, 12 H), 1.11 (t, J = 7.0, 12 H), 0.87 (d, J = 5.1, 6 H); ^{13}C NMR (75 MHz, CDCl_3): δ = 174.9 (C), 131.0 (C), 124.7 (CH), 73.6 (C), 42.0 (CH_2), 41.4 (CH_2), 37.9 (CH_2), 36.9 (CH_2), 36.8 (CH_2), 32.5 (CH), 30.5 (CH_2), 30.4 (CH_2), 26.6 (CH_3), 25.6 (CH_3), 25.3 (CH_2), 19.4 (CH_3), 17.5 (CH_3), 13.9 (CH_3), 12.4 (CH_3); MS (70 eV): m/z (%): 283 [M] $^+$ (10), 183 (5), 144 (12), 83 (16), 69 (58); HRMS calcd for $\text{C}_{17}\text{H}_{33}\text{NO}_2$ 283.2511, found 283.2507; IR (neat): $\tilde{\nu}$ = 3387, 1614 cm^{-1} ; R_f = 0.5 (hexane/AcOEt 1/1).

















