Direct Catalytic Synthesis of Enantiopure 5-Substituted Oxazolidinones From Racemic Terminal Epoxides

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General Methods. The ¹H and ¹³C NMR spectra were recorded at 400 MHz and 100 MHz, respectively. The chemical shifts (δ) for ¹H and ¹³C are given in ppm relative to residual signals of the solvent (CHCl₃). Coupling constants are given in Hz. Carbon types were determined from DEPT ¹³C NMR experiments. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad signal. Purification of reaction products was carried out by flash chromatography (FC) on silica gel (230–400 mesh). Melting points are uncorrected. Optical rotations are reported as follows: [α]_D^t (c in g per 100 mL, solvent).

Materials. Commercial grade reagents and solvents were used without further purification; otherwise, where necessary, they were purified as recommended.¹

Racemic epoxides: 1,2-epoxy butane **2a**, propylene oxide **2b**, 1,2-epoxy-7-octene **2c**, isopropyl glycidyl ether **2f**, and styrene oxide **2h** were purchased from Aldrich and used as received. *O*-silylated epoxide **2g** was prepared by protection of racemic glycidol (CH₂Cl₂ / imidazole / *tert*-butyldimethylsilyl chloride). Other racemic epoxides **2d-e**, **2i-k** were prepared by *m*-CPBA oxidation of the corresponding alkenes.²

Urethane **3** was purchased from Aldrich and used as received.

N-Boc-2-nitrobenzenesulfonamide **6** was prepared according to literature procedure.³

Both (R,R) and (S,S)-(salen)-Co(II) complexes **1** (Aldrich) are commercially available.

Determination of Enantiomeric Purity. Chiral HPLC analysis was performed on an Agilent 1100-series instrumentation. Daicel Chiralcel OD and Chiralpak AD-H, OB-H or AS-H columns with *i*-PrOH/hexane as the eluent were used.

Chiral GC analysis was performed on a Hewlett-Packard 5890 gas chromatography using a RT-BetaDEX-sm chiral column.

The enantiomeric excess (ee) of the products was determined by HPLC analysis on the oxazolidinones **4h-k** and on the corresponding *N*-benzoyl derivatives for oxazolidinones **4c-e** and **4g**. The enantiomeric excess (ee) of the oxazolidinones **4a-b** and **4f** was determined by GC analysis. HPLC and GC traces were compared to racemic samples prepared with racemic (salen)-Co^{III} complex as the catalyst.

Determination of Regiochemistry. The regiochemistry of the ring opening reactions was determined by careful GC and NMR analysis of the crude reaction mixtures and by comparison with literature data.

Determination of Absolute Configuration. The measured optical rotation of oxazolidinones **4b**,⁴ and **4h**,⁵ were compared with the literature value. All other absolute configurations were assigned by analogy.

¹ Armarengo, W. L. F.; Perrin, D. D.; In *Purification of Laboratory Chemicals*, 4th ed.; Butterworth Heinemann: Oxford, 1996.

² Moyna, G.; Williams, H. J.; Scott, A. L. *Synth. Commun.* **1996**, 26, 2235.

³ Fukuyama, T.; Cheung, M.; Kan, T. *Synlett* **1999**, 1301.

⁴ Nishiyama, T.; Matsui, S.; Yamada, F. *J. Heterocycl. Chem.* **1986**, 23, 1427.

⁵ Matsumura, Y.; Ohishi, T.; Sonoda, C.; Maki, T.; Watanabe, M. *Tetrahedron*, **1997**, 53, 4579.

Calculation of conversion (c) and evaluation of selectivity factor s .⁶ Evaluation of selectivity factor s was accomplished by using the equation: $s = k_{rel} = \ln[1 - c(1+ee)]/\ln[1 - c(1-ee)]$, where ee is the enantiomeric excess of the oxazolidinone product and c is the conversion. The conversion was set to equal the isolated yield of the oxazolidinone product, after the sequential one-pot cyclization of the corresponding amino alcohol, so calculated values for c actually represent lower limits: the value for c was calculated by multiplying the isolated yield times 0.476 for entries 1-3 and 5-7 (2.1 equiv of epoxides used) and times 0.454 for entries 4 and 8-11 (2.2 equiv of epoxides used) (Table S1).

Indeed, the s values in table S1 represent just an evaluation of the efficiency of the presented methodology, that stems from the extraordinary level of selectivity of the carbamate-based Aminolytic Kinetic Resolution (AKR) strategy: the exact calculation of the selectivity factors should be done on the amino alcohol products.⁷ The evaluation of the selectivity on the oxazolidinone products should imply that the cyclization of the corresponding aminols proceeds without racemization. While this is true for aliphatic substrates, we have observed that the enantiopurity of the aromatic oxazolidinones is slightly affected by the cyclization step (the corresponding aminols are produced in enantiomerically pure form, ee > 99%)

Table S1. Evaluation of s Values for the Direct Conversion of Terminal Epoxides to Enantiopure Oxazolidinones **4**.

Entry	R	product	yield	c	ee	s
1	Et	4a	0.94	0.447	99.9	>3000
2	Me	4b	0.97	0.471	99.9	>3000
3	(CH ₂) ₄ CH=CH ₂	4c	0.95	0.452	99.7	1715
4	<i>c</i> -C ₆ H ₁₁	4d	0.97	0.461	99.2	680
5	CH ₂ Ph	4e	0.98	0.466	99.5	670
6	CH ₂ O(<i>i</i> -Pr)	4f	0.90	0.428	99.5	900
7	CH ₂ OTBS	4g	0.92	0.438	99.0	465
8	Ph	4h	0.90	0.428	99.2	560
9	4-ClPh	4i	0.98	0.466	98.7	428
10	3-ClPh	4j	0.97	0.461	96.5	145
11	3-NO ₂ Ph	4k	0.94	0.447	97.5	190

Considering the extraordinarily levels of selectivities ($s > 145$) observed, the relative magnitude of s factors can provide useful guidelines of evaluation of the presented strategy, but the absolute values for the best substrates (s exceeding 3000) are certainly lacking precision.

⁶ Kagan, H. B.; Fiaud, J. C. In *Topics in Stereochemistry*; Allinger, N. L.; Eliel, E. L. Eds.; Interscience: New York, 1987; Vol. 14, p 249.

⁷ For an exact calculation of the selectivity of the AKR, see: Bartoli, G.; Bosco, M.; Carlone, A.; Locatelli, M.; Melchiorre, P.; Sambri, L. *Org. Lett.* **2004**, *6*, 3973 and Supporting Information therein.

Experimental Procedures.

General Procedure for the *N*-Benzoylation of Oxazolidinones **4c-e and **4g**.** Under an inert atmosphere, pure oxazolidinones **4c-e**, **g** were dissolved in THF followed by the addition of benzoyl chloride (1.3 equiv) and NaH (1.1 equiv) at 0°C. The reaction mixture was allowed to rise to room temperature, stirred for 3 hours and quenched with NaHCO₃, extracted with Et₂O and dried over anhydrous MgSO₄. Purification by flash chromatography (hexane/AcOEt 9/1) afforded pure *N*-benzoyl oxazolidinones.

General Procedure for the Direct Conversion of Racemic Terminal Epoxides to Enantiopure Oxazolidinones. All the reactions were carried out in undistilled solvent without any precautions to exclude water. In an ordinary test tube equipped with a magnetic stirring bar, the (salen)-Co^{II} complex **1** (x mol% relative to racemic epoxide, x = 1.5-5) was dissolved in 0.15 mL of TBME. After addition of the oxidizing agent (*p*-nitrobenzoic acid, 2x mol%), the tube was closed with a rubber stopper and the mixture was stirred at room temperature over which time the color changed from orange-red to dark brown. Then the urethane **3** (44.5 mg, 0.5 mmol) was added. After 5 minutes stirring, racemic epoxide **2** (1.05 mmol or 1.1 mmol) was added and stirring was continued at room temperature till the completion of the AKR step, as indicated by TLC analysis, at which time 5 mL of THF and 1 mmol of NaH (24 mg) were added. After 3 h stirring, the crude reaction mixture was quenched with NH₄Cl and diluted with Et₂O. The organic layer was washed with brine and dried over Na₂SO₄. After filtration, solvent was removed *in vacuo*, and the residue was purified by flash chromatography to yield the 5-substituted oxazolidinone **4a-k** in almost enantiomerically pure form.

(S)-5-Ethyl-oxazolidin-2-one (4a) – The reaction was carried out at room temperature following the general procedure for 18 h using 1.5 mol% of (*R,R*)-(salen)Co^{II} **1** and 3 mol% of *p*-nitrobenzoic acid as the oxidizing agent, 0.5 mmol of urethane **3** and 1.05 mmol of racemic 1,2-epoxy butane **2a**. After the cyclization step, the title compound was isolated by column chromatography (DCM/AcOEt 6/4) as a white solid in 94% yield; melting point: 51-53 °C. The ee was determined by GC analysis (isotherm 150 °C; τ_R = 19.6 min; τ_S = 20.1 min). $[\alpha]_D^{25}$ = -14.7° (*c* = 1, CHCl₃, 99.9% ee). ESI-MS *m/z* 114 [M-H]⁻. ¹H NMR (CDCl₃): δ = 1.01 (t, 3H, *J* = 7.5), 1.65 -1.87 (m, 2H), 3.25 (ddd, *J* = 1.2, 7.2, 8.4, 1H), 3.66 (ddd, *J* = 1.2, 8.4, 8.4, 1H), 4.55-4.62 (m, 1H), 5.30 (bs, 1H, NH); ¹³C NMR (CDCl₃): δ = 8.7 (CH₃), 27.8 (CH₂), 45.5 (CH₂), 78.2 (CH), 160.3 (C).

(S)-5-Methyl-oxazolidin-2-one (4b)⁸ – The reaction was carried out following the general procedure at room temperature for 18 h using 1.5 mol% of (*R,R*)-(salen)Co^{II} **1** and 3 mol% of *p*-nitrobenzoic acid as the oxidizing agent, 0.5 mmol of urethane **3** and 1.05 mmol of racemic propylene oxide **2b**. After the cyclization step, the title compound was isolated by column chromatography (DCM/AcOEt 3/7) as a colourless oil in 97% yield. The ee was determined by GC analysis (isotherm 145 °C; τ_R = 15.1 min; τ_S = 15.5 min). $[\alpha]_D^{25}$ = -8.9° (c = 1.0, CHCl₃, 99.9% ee), lit.⁴ $[\alpha]_D^{25}$ = -20.9°, (*S*)-**4b**. ESI-MS m/z 102 [M+H]⁺, 124 [M+Na]⁺. ¹H NMR (CDCl₃): δ = 1.45 (d, 3H, J = 6.2), 3.19 (ddd, J = 0.8, 7.2, 8.4, 1H), 3.69 (ddd, J = 0.8, 8.4, 8.4, 1H), 4.73-4.81 (m, 1H), 5.58 (bs, 1H, NH); ¹³C NMR (CDCl₃): δ = 20.8 (CH₃), 47.7 (CH₂), 73.8 (CH), 160.5 (C).

(S)-5-Hex-5-enyl-oxazolidin-2-one (4c) – The reaction was carried out following the general procedure at room temperature for 18 h using 1.5 mol% of (*R,R*)-(salen)Co^{II} **1** and 3 mol% of *p*-nitrobenzoic acid as the oxidizing agent, 0.5 mmol of urethane **3** and 1.05 mmol of racemic 1,2-epoxy-7-octene **2c**. After the cyclization step, the title compound was isolated by column chromatography (DCM/AcOEt 8/2) as a white solid in 95% yield; melting point: 63-65 °C. The ee was determined by HPLC analysis on the corresponding *N*-benzoyl derivative, prepared following the described general procedure, using a Chiralpak AD-H column (90/10 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_R = 20.4 min; τ_S = 24.5 min). $[\alpha]_D^{25}$ = -23.0° (c = 2.0, CHCl₃, 99.7% ee). ESI-MS m/z 168 [M-H]⁻. ¹H NMR (CDCl₃): δ = 1.32-1.55 (m, 4H), 1.59-1.71 (m, 1H), 1.76-1.86 (m, 1H), 2.04-2.10 (m, 2H), 3.23 (ddd, J = 0.8, 7.2, 8.4, 1H), 3.66 (ddd, J = 0.8, 8.4, 8.4, 1H), 4.60-4.67 (m, 1H), 4.94-5.04 (m, 2H), 5.13 (bs, 1H, NH), 5.74-5.84 (m, 1H); ¹³C NMR (CDCl₃): δ = 24.0 (CH₂), 28.4 (CH₂), 33.4 (CH₂), 34.7 (CH₂), 45.9 (CH₂), 77.1 (CH), 114.7 (CH), 138.3 (CH₂), 160.2 (C).

(S)-5-Cyclohexyl-oxazolidin-2-one (4d) – The reaction was carried out following the general procedure at room temperature for 40 h using 4 mol% of (*R,R*)-(salen)Co^{II} **1**, 8 mol% of *p*-nitrobenzoic acid as the additive, 0.5 mmol of urethane **3** and 1.1 mmol of racemic epoxide **2d**. After the cyclization step, the title compound was isolated by column chromatography (DCM/AcOEt 7/3) as a white solid in 97% yield; melting point: 130-131 °C. The ee was determined by HPLC analysis on the corresponding *N*-benzoyl derivative, prepared following the described general procedure, using a Chiralpak AD-H column (85/15 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_R = 18.7 min; τ_S = 28.2 min). $[\alpha]_D^{25}$ = -35.8 (c = 1.0, CHCl₃, 99.2% ee). ESI-MS m/z 170 [M+H]⁺, 192 [M+Na]⁺. ¹H

⁸ Gabriel, B.; Mancuso, R.; Salerno, G.; Costa, M. *J. Org. Chem.* **2003**, 68, 601.

NMR (CDCl₃): δ = 1.00-1.30 (m, 5H), 1.58 -1.80 (m, 5H), 1.93-1.96 (m, 1H), 3.32-3.36 (m, 1H), 3.58 (ddd, J = 0.8, 8.4, 8.4, 1H), 4.33-4.39 (m, 1H) 5.05 (bs, 1H, NH); ¹³C NMR (CDCl₃): δ = 25.3 (CH₂), 25.5 (CH₂), 26.1 (CH₂), 27.3 (CH₂), 27.9 (CH₂), 42.0 (CH), 43.9 (CH₂), 81.0 (CH), 160.4 (C).

(S)-5-Benzyl-oxazolidin-2-one (4e) – The reaction was carried out following the general procedure at room temperature for 40 h using 4 mol% of (*R,R*)-(salen)Co^{II} **1**, 8 mol% of *p*-nitrobenzoic acid as the additive, 0.5 mmol of urethane **3** and 1.05 mmol of racemic epoxide **2e**. After the cyclization step, the title compound was isolated by column chromatography (DCM/AcOEt 65/35) as a white solid in 98% yield; melting point: 107-109 °C. The ee was determined by HPLC analysis on the corresponding *N*-benzoyl derivative, prepared following the described general procedure, using a Chiralpak AS-H column (80/20 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_R = 27.6 min; τ_S = 37.2 min). $[\alpha]_D^{25}$ = -20.2° (c = 0.9, CHCl₃, 99.5% ee). ESI-MS m/z 176 [M-H]⁻. ¹H NMR (CDCl₃): δ = 2.94 (dd, J = 6.8, 14.0, 1H), 3.15 (dd, J = 6.0, 14.0, 1H), 3.33 (ddd, J = 0.8, 7.2, 8.4, 1H), 3.58 (ddd, J = 0.8, 8.4, 8.4, 1H), 4.83-4.90 (m, 1H), 5.59 (bs, 1H, NH), 7.21-7.34 (m, 5H); ¹³C NMR (CDCl₃): δ = 40.6 (CH₂), 45.0 (CH₂), 77.1 (CH), 127.1 (CH), 128.7 (CH, 2), 129.3 (CH, 2), 135.2 (C), 159.8 (C).

(R)-5-Isopropoxymethyl-oxazolidin-2-one (4f) – The reaction was carried out following the general procedure at room temperature for 24 h using 2 mol% of (*R,R*)-(salen)Co^{II} **1** and 4 mol% of *p*-nitrobenzoic acid as the oxidizing agent, 0.5 mmol of urethane **3** and 1.05 mmol of racemic isopropyl glycidyl ether **2f**. After the cyclization step, the title compound was isolated by column chromatography (DCM/AcOEt 6/4) as a colourless oil in 90% yield. The ee was determined by GC analysis (isotherm 170 °C; τ_S = 19.6 min; τ_R = 20.4 min). $[\alpha]_D^{25}$ = -7.6° (c = 1.8, CHCl₃, 99.5% ee). ESI-MS m/z 158 [M-H]⁻. ¹H NMR (CDCl₃): 1.16 (d, 6H, J = 6.15), 3.45-3.50 (m, 1H), 3.55-3.70 (m, 4H), 4.69-4.75 (m, 1H), 5.31 (bs, 1H, NH); ¹³C NMR (CDCl₃): δ = 21.8 (CH₃, 2C), 42.8 (CH₂), 68.4 (CH₂), 72.6 (CH), 75.3 (CH), 160.1 (C).

(R)-5-(tert-Butyl-dimethyl-silanyloxymethyl)-oxazolidin-2-one (4g) – The reaction was carried out following the general procedure at room temperature for 36 h using 3 mol% of (*R,R*)-(salen)Co^{II} **1**, 6 mol% of *p*-nitrobenzoic acid as the additive, 0.5 mmol of urethane **3** and 1.05 mmol of racemic epoxide **2g**.

After the cyclization step, the title compound was isolated by column chromatography (DCM/AcOEt 65/35) as a white solid in 92% yield; melting point: 56-58 °C. The ee was determined by HPLC analysis on the corresponding *N*-benzoyl derivative, prepared following the described general procedure, using a Chiralpak AD-H column (80/20 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_S 8.4 min; τ_R = 9.0 min). $[\alpha]_D^{25}$ = -4.7° (c = 1.06, CHCl₃, 99.0% ee). ESI-MS m/z 232 [M+H]⁺, 254 [M+Na]⁺. ¹H NMR (CDCl₃): δ = 0.08 (s, 6H, 2 CH₃), 0.88 (s, 9H, 3 CH₃), 3.57 (ABX, J = 8.6, 8.6, 2H), 3.77 (ABX, J = 4.8, 11.2, 2H), 4.63-4.70 (m, 1H), 5.56 (bs, 1H, NH); ¹³C NMR (CDCl₃): δ = -5.5 (CH₃, 2C), 18.1 (C), 25.7 (CH₃, 3C), 42.1 (CH₂), 63.4 (CH₂), 76.3 (CH), 160.4 (C).

(S)-5-Phenyl-oxazolidin-2-one (4h)⁵ – The reaction was carried out following the general procedure at room temperature for 40 h using 4 mol% of (*R,R*)-(salen)Co^{II} **1**, 8 mol% of *p*-nitrobenzoic acid as the additive, 0.5 mmol of urethane **3** and 1.1 mmol of racemic styrene oxide **2h**. After the cyclization step, the title compound was isolated by column chromatography (DCM/AcOEt 8/2) as a white solid in 90% yield; melting point: 92-93 °C. The ee was determined by HPLC analysis using a Chiralcel OD column (90/10 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_S = 29.5 min; τ_R = 40.2 min). $[\alpha]_D^{25}$ = +22.6° (c = 0.93, CHCl₃, 99.2% ee), lit.⁴ $[\alpha]_D^{25}$ = +10.0°, (S)-**4h**. ESI-MS m/z 162 [M-H]⁻. ¹H NMR (CDCl₃): δ = 3.55 (ddd, J = 0.8, 7.6, 8.6, 1H), 3.98 (ddd, J = 0.8, 8.6, 8.6, 1H), 5.50 (bs, 1 H, NH), 5.63 (t, J = 8.6, 1H), 7.35-7.43 (m, 5H); ¹³C NMR (CDCl₃): δ = 48.3 (CH₂), 77.9 (CH), 125.6 (CH, 2C), 128.9 (CH, 3C), 138.4 (C), 159.9 (C).

(S)-5-(4-Chloro-phenyl)-oxazolidin-2-one (4i) – The reaction was carried out at room temperature for 60 h using 5 mol% of (*R,R*)-(salen)Co^{II} **1**, 8 mol% of *p*-nitrobenzoic acid as the additive, 0.5 mmol of urethane **3** and 1.1 mmol of racemic epoxide **2i**. The cyclization was accomplished by adding THF (0.1M) and *tert*-BuOK (2 equiv). After 16 h stirring, the crude reaction mixture was quenched with NH₄Cl and diluted with Et₂O. The organic layer was washed with brine and dried over Na₂SO₄. After filtration, solvent was removed in vacuo, and the title compound was isolated by column chromatography (DCM/AcOEt 7/3) as a white solid in 98% yield; melting point: 129-132 °C. The ee was determined by HPLC analysis using a Chiralcel OD column (90/10 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_S = 35.3 min; τ_R = 40.8 min). $[\alpha]_D^{25}$ = +34.2° (c = 1.05, CHCl₃, 98.7% ee). ESI-MS m/z 196 [M-H]⁻. ¹H NMR (CDCl₃): δ = 3.50 (ddd, J = 0.8, 7.6, 8.4, 1H), 3.98 (ddd, J = 0.8, 8.4, 8.4, 1H), 5.60 (t, J = 8.4, 1H), 5.85 (bs, 1 H, NH),

7.30-7.40 (m, 4H); ^{13}C NMR (CDCl_3): δ = 48.2 (CH_2), 77.1 (CH), 127.0 (CH, 2C), 129.1 (CH, 2C), 134.8 (C), 136.9 (C), 159.7 (C).

(S)-5-(3-Chloro-phenyl)-oxazolidin-2-one (4j) – The reaction was carried out following the general procedure at room temperature for 60 h using 5 mol% of (*R,R*)-(salen) Co^{II} **1**, 8 mol% of *p*-nitrobenzoic acid as the additive, 0.5 mmol of urethane **3** and 1.1 mmol of racemic epoxide **2j**. After the cyclization step, the title compound was isolated by column chromatography (DCM/AcOEt 7/3) as a white solid in 97% yield; melting point: 114-116 °C. The ee was determined by HPLC analysis using a Chiralcel OD column (90/10 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_{S} = 32.0 min; τ_{R} = 42.1 min). $[\alpha]_{\text{D}}^{25}$ = +37.2° (c = 1.07, CHCl_3 , 96.5% ee). ESI-MS m/z 196 $[\text{M-H}]^-$. ^1H NMR (CDCl_3): δ = 3.51 (ddd, J = 0.8, 7.6, 8.4, 1H), 4.00 (ddd, J = 0.8, 8.4, 8.4, 1H), 5.60 (t, J = 8.4, 1H), 5.82 (bs, 1 H, NH), 7.25-7.40 (m, 4H); ^{13}C NMR (CDCl_3): δ = 48.1 (CH_2), 76.9 (CH), 123.6 (CH), 125.8 (CH), 129.0 (CH), 130.2 (CH), 134.9 (C), 140.5 (C), 159.7 (C).

(S)-5-(3-Nitro-phenyl)-oxazolidin-2-one (4k) – The reaction was carried out following the general procedure at room temperature for 60 h using 5 mol% of (*R,R*)-(salen) Co^{II} **1**, 8 mol% of *p*-nitrobenzoic acid as the additive, 0.5 mmol of urethane **3** and 1.1 mmol of racemic epoxide **2k**. After the cyclization step, the title compound was isolated by column chromatography (DCM/AcOEt 7/3) as a white solid in 94% yield; melting point: 101-103 °C. The ee was determined by HPLC analysis using a Chiralpak OB-H column (70/30 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_{R} = 45.4 min; τ_{S} = 52.3 min). $[\alpha]_{\text{D}}^{25}$ = +15.5° (c = 1.0, CHCl_3 , 97.5% ee). ESI-MS m/z 207 $[\text{M-H}]^-$. ^1H NMR (CDCl_3): δ = 3.56 (ddd, J = 0.8, 7.6, 8.4, 1H), 4.10 (ddd, J = 0.8, 8.4, 8.4, 1H), 5.43 (bs, 1 H, NH), 5.74 (t, J = 8.4, 1H), 7.61-7.66 (m, 1H), 7.75-7.78 (m, 1H), 8.23-8.27 (m, 2H); ^{13}C NMR (CDCl_3): δ = 48.0 (CH_2), 76.4 (CH), 120.7 (CH), 123.9 (CH), 130.2 (CH), 131.5 (CH), 140.6 (C), 148.5 (C), 159.1 (C).

Enantioconvergent Strategy for the Total Conversion of Racemic Epoxide into a Single Enantiopure Oxazolidinone.

Total conversion of racemic **2a** into enantiopure oxazolidinone **4a**.

The reaction was carried out in undistilled solvent without any precautions to exclude water. In an ordinary test tube equipped with a magnetic stirring bar, the (salen)- Co^{II} complex **1** (24 mg, 0.04 mmol) was dissolved in 0.15 mL of TBME. After addition of the oxidizing agent (*p*-nitrobenzoic acid, 13.3 mg, 0.08 mmol), the tube was closed with a rubber stopper and the mixture was stirred at room temperature over which time the color changed from orange-red to dark brown. Then the urethane **3** (89 mg, 1 mmol) was added. After 5 minutes stirring, epoxide **2a** (144 mg, 2 mmol) was added and stirring was continued at room temperature for 30 h, at which time 0.15 mL of TBME and *N*-Boc sulfonamide **6** (301 mg, 1 mmol) were added. After 3 h the crude reaction mixture was directly charged on the column chromatography and purified (DCM/AcOEt from 95/5 to 8/2) to yield the isolated pseudo-enantiomeric aminols **5a** and **7a**.

Et
 OH
 NHCOOEt
(S)-2-Hydroxy-butyl-carbamic acid ethyl ester (5a) – The title compound was isolated by column chromatography (DCM/AcOEt 8/2, $R_f = 0.2$) in 84% yield as a colourless liquid. $[\alpha]_{\text{D}}^{25} = +20.6^\circ$ ($c = 1.1$, CHCl_3). ESI-MS m/z 160 $[\text{M-H}]^-$, 184 $[\text{M}+\text{Na}]^+$. ^1H NMR (CDCl_3): $\delta = 0.95$ (t, $J = 7.2$, 3H), 1.23 (t, $J = 7.0$, 3H), 1.41-1.53 (m, 2H), 2.57 (bs, 1H, OH), 3.00-3.10 (m, 1H), 3.29-3.39 (m, 1H), 3.55-3.65 (m, 1H), 4.11 (q, J

= 7.2, 2H), 5.17 (bs, 1 H, NH); ^{13}C NMR (CDCl_3): δ = 9.7 (CH_3), 14.5 (CH_3), 27.5 (CH_2), 46.4 (CH_2), 60.8 (CH_2), 72.5 (CH), 157.4 (C).

***N*-2-nitrobenzensulfonyl-((*R*)-2-Hydroxy-butyl)-carbamic acid *tert*-butyl ester (**7a**)** – The title compound was isolated by column chromatography

(DCM/AcOEt 8/2, R_f = 0.6) in 98% yield as a white solid, melting point: 81–83 °C. The ee was determined by HPLC analysis using a Chiralpak AD-H column (8/2 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_R = 26.2 min; τ_S = 35.5 min). $[\alpha]_D^{25}$ = +26.6° (c = 2.0, CHCl_3 , 99.5% ee). ESI-MS m/z 373 $[\text{M}-\text{H}]^-$. ^1H NMR (CDCl_3): 1.03 (t, J = 7.0, 3H), 1.34 (s, 9H), 1.48–1.64 (m, 2H), 2.00 (d, J = 6.0, OH), 3.79–3.89 (m, 3H), 7.73–7.79 (m, 3H), 8.34–8.38 (m, 1H); ^{13}C NMR (CDCl_3): δ = 9.8 (CH_3), 27.8 (CH_3 , 3C), 27.9 (CH_2), 53.1 (CH_2), 72.1 (CH), 85.5 (C), 124.4 (CH), 131.8 (CH), 133.1 (CH), 133.6 (C), 134.1 (CH), 147.6 (C), 150.8 (C).

Cyclization of 5a to Oxazolidinone 4a with Retention of Configuration: Pure amino alcohol **5a** (136 mg, 0.84 mmol) was dissolved in THF (8.5 mL) and NaH (40 mg, 1.7 mmol) was added at room temperature. After being stirred for 3 hours, the mixture was diluted with Et_2O and the reaction was quenched with some drops of methanol. The mixture was washed with NH_4Cl , extracted with Et_2O and dried over anhydrous MgSO_4 . Evaporation of the solvent affords pure oxazolidinone **4a** in quantitative yield (96.5 mg) and in enantiopure form (ee > 99%).

Cyclization of 7a to Oxazolidinone 4a with Inversion of Configuration (one-pot reaction sequence):

- 1) Deprotection of the Nosyl group:**⁹ pure amino alcohol **7a** (366 mg, 0.98 mmol) was dissolved in CH_3CN (10 mL), followed by the addition of 1.1 equiv of thiophenol (110 μL , 1.08 mmol) and 2 equiv of K_2CO_3 (270.5 mg, 1.96 mmol). After being stirred for 1 hour at room temperature, 1 equiv of K_2CO_3 (135.2 mg, 0.98 mmol) and 1 equiv of thiophenol (108 μL , 0.98 mmol) were added. After being stirred overnight, the end of the deprotection step was monitored by TLC analysis.
- 2) Subsequent One-pot Cyclization with Stereoinversion:**¹⁰ The stereoinversion was achieved by directly adding THF (10 mL) and 5 equiv of SOCl_2 (356 μL , 4.9 mmol).

⁹ Fukuyama, T.; Cheung, M.; Jow, C.-K.; Hidai Y.; Kan, T. *Tetrahedron Lett.* **1997**, 38, 5831.

¹⁰ Ghosh, A. K.; Shin, D.; Mathivanan, P. *Chem. Commun.* **1999**, 1025.

After being stirred at room temperature for 6 hours, the mixture was diluted with AcOEt and quenched with 10 mL of brine. After extraction of the aqueous layer with AcOEt, the organic layers were collected and dried over anhydrous MgSO₄. The title compound **4a** was isolated by column chromatography (DCM/AcOEt 6/4, R_f = 0.3) in enantiomerically pure form (ee>99%) and in 79% yield (89 mg) as a white solid.

Both the cyclization steps afforded the same enantiomer of the oxazolidinone **4a** in 81% overall yield (186 mg) starting from the racemic 1,2-epoxy butane **2a** and in 99.2% ee.

Total conversion of racemic **2c** into enantiopure oxazolidinone **4c**.

The reaction was carried out in undistilled solvent without any precautions to exclude water. In an ordinary test tube equipped with a magnetic stirring bar, the (salen)-Co^{II} complex **1** (24 mg, 0.04 mmol) was dissolved in 0.15 mL of TBME. After addition of the oxidizing agent (*p*-nitrobenzoic acid, 13.3 mg, 0.08 mmol), the tube was closed with a rubber stopper and the mixture was stirred at room temperature over which time the color changed from orange-red to dark brown. Then the urethane **3** (89 mg, 1 mmol) was added. After 5 minutes stirring, epoxide **2c** (252 mg, 2 mmol) was added and stirring was continued at room temperature for 30 h, at which time 0.2 mL of TBME and *N*-Boc sulfonamide **6** (302 mg, 1 mmol) were added. After 3 h the crude reaction mixture was directly charged on the column chromatography and purified (DCM/AcOEt from 99/1 to 7/3) to yield the isolated pseudo-enantiomeric aminols **5c** and **7c**.

((S)-2-Hydroxy-oct-7-enyl)-carbamic acid ethyl ester (5c**) –**

The title compound was isolated by column chromatography (DCM/AcOEt 8/2, R_f = 0.25) in 94% yield (202 mg, 0.94 mmol) as a white solid, melting point = 38-40 °C. $[\alpha]_D^{25}$ = +11.3° (c = 1.1, CHCl₃). ESI-MS m/z 214 [M-H]⁻, 238 [M+Na]⁺. ¹H NMR (CDCl₃): δ = 1.25 (t, J = 7.2, 3H), 1.35-1.50 (m, 6H), 2.03-2.10 (m, 2H), 2.17 (bs, 1H, OH), 3.01-3.09 (m, 1H), 3.32-3.40 (m, 1H), 3.66-3.74 (m, 1H), 4.12 (q, J = 7.2, 2H), 4.92-5.07 (m, 3H, 1 NH), 5.74-5.85 (m, 1H); ¹³C NMR (CDCl₃): δ = 14.5 (CH₃), 24.9 (CH₂), 28.7 (CH₂), 33.5 (CH₂), 34.4 (CH₂), 46.8 (CH₂), 60.9 (CH₂), 71.1 (CH), 114.4 (CH₂), 136.6 (CH), 157.4 (C).

***N*-2-nitrobenzensulfonyl-(R)-2-Hydroxy-oct-7-enyl)-carbamic acid *tert*-butyl ester (**7c**) –**

The title compound was isolated by column chromatography (DCM/AcOEt 8/2, R_f = 0.7) in 98% yield (419 mg, 0.98 mmol) as a white solid, melting point: 103-105 °C. The ee was determined by HPLC analysis using a Chiralpak AD-H column (8/2 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_R = 22.1 min; τ_S = 31.8

min). $[\alpha]_D^{25} = +27.2^\circ$ ($c = 2.05$, CHCl_3 , 99.7% ee). ESI-MS m/z 427 $[\text{M}-\text{H}]^-$. ^1H NMR (CDCl_3): $\delta = 1.34$ (s, 9H), 1.40-1.58 (m, 6H), 2.0 (d, $J = 6.4$, 1H, OH), 2.05-2.11 (m, 2H), 3.76-3.86 (m, 2H), 3.87-3.95 (m, 1H), 4.92-5.04 (m, 2H), 5.76-5.86 (m, 1H), 7.73-7.77 (m, 3H), 8.34-8.38 (m, 1H); ^{13}C NMR (CDCl_3): $\delta = 24.7$ (CH_2), 26.6 (CH_3 , 3C), 28.6 (CH_2), 33.5 (CH_2), 34.6 (CH_2), 53.2 (CH_2), 70.5 (CH), 85.4 (C), 114.3 (CH_2), 124.3 (CH), 131.7 (CH), 132.8 (CH), 133.3 (C), 134.6 (CH), 138.6 (CH), 147.4 (C), 150.6 (C).

Cyclization of 5c to Oxazolidinone 4c with Retention of Configuration: Pure amino alcohol **5c** (202 mg, 0.94 mmol) was dissolved in THF (10 mL) and NaH (46 mg, 1.9 mmol) was added at room temperature. After being stirred for 3 hours, the mixture was diluted with Et_2O and the reaction was quenched with some drops of methanol. The mixture was washed with NH_4Cl , extracted with Et_2O and dried over anhydrous MgSO_4 . Evaporation of the solvent affords pure oxazolidinone **4c** in 98% yield (155.5 mg) and in enantiopure form (ee = 98.9%).

Cyclization of 7c to Oxazolidinone 4c with Inversion of Configuration:

The one-pot reaction sequence afforded the oxazolidinone **4c** with inversion of configuration in 98.0% ee and in 61% yield (101 mg). In this case, the isolation of the deprotected aminol **8** followed by subsequent cyclization proved to be a better protocol.

- 1) *Deprotection of the Nosyl group:*⁹ Pure amino alcohol **7c** (419 mg, 0.98 mmol) was dissolved in CH_3CN (10 mL), followed by the addition of 1.1 equiv of thiophenol (110 μL , 1.08 mmol) and 2 equiv of K_2CO_3 (270.5 mg, 1.96 mmol). After being stirred for 1 hour at room temperature, 1 equiv of K_2CO_3 (135.2 mg, 0.98 mmol) and 1 equiv of thiophenol (108 μL , 0.98 mmol) were added. After being stirred overnight, the end of the deprotection step was monitored by TLC analysis. The mixture was quenched with brine, extracted with AcOEt and dried over anhydrous MgSO_4 . Evaporation of the solvent followed by flash chromatography (DCM/AcOEt 8/2) affords pure aminol **8** in 71% yield (169 mg).
- 2) *Subsequent One-pot Cyclization with Stereoinversion:*¹⁰ Pure aminol **8** was dissolved in THF (10 mL) and 5 equiv of SOCl_2 (356 μL , 4.9 mmol) was added. After being stirred at room temperature for 16 hours, the mixture was diluted with AcOEt and quenched with 10 mL of brine. After extraction with AcOEt , the organic layers were collected and

dried over anhydrous MgSO_4 . The title compound was isolated by column chromatography (DCM/AcOEt 8/2) in quantitative yield (118 mg) and 99.9% ee.

Both the cyclization steps afforded the same enantiomer of the oxazolidinone **4c** in 82% overall yield (273.5 mg) starting from racemic 1,2-epoxy-7-octene **2c** and in >99% ee.

HPLC and GC Traces

Chiral GC: RT-BetaDEX-sm, isotherm 150 °C

Retention Times	Area	Area Percent
19.686	nd	0
20.111	$5.52603 \cdot 10^4$	99.99
Totals	$5.52603 \cdot 10^4$

Chiral GC: RT-BetaDEX-sm, isotherm 145 °C

Retention Times	Area	Area Percent
15.207	nd	0
15.559	$5.53331 \cdot 10^4$	99.99
Totals	$5.53331 \cdot 10^4$

HPLC: CHIRALPAK AD-H 90/10 hexane/*iso*-propanol, 0.75 mL/min

Retention Times	Area	Area Percent
20.376	59187	0.1192
24.481	49604768	99.8808
Totals	49663955

HPLC: CHIRALPAK AD-H 85/15 hexane / *iso*-propanol, 0.75 mL/min

Retention Times	Area	Area Percent
18.458	38.02682	0.4106
27.691	9222.43457	99.5894
Totals	9260.46139

HPLC: CHIRALPAK AS-H 80/20 hexane / *iso*-propanol, 0.75 mL

Retention Times	Area	Area Percent
27.548	115780	0.2694
37.203	42862712	99.7306
Totals	42978492

Chiral GC: RT-BetaDEX-sm, isotherm 170 °C

Retention Times	Area	Area Percent
20.021	512.57257	0.24953
20.969	$2.04899 \cdot 10^5$	99.75047
Totals	$2.05412 \cdot 10^5$

HPLC: CHIRALPAK AD-H 80/20 hexane / *iso*-propanol, 0.75 mL

Retention Times	Area	Area Percent
8.448	222.97833	0.5195
9.066	4.26955 · 10 ⁴	99.4805
Totals	4.29184 · 10 ⁴

HPLC: CHIRALCEL OD 90/10 hexane / *iso*-propanol, 0.75 mL

Retention Times	Area	Area Percent
29.720	$1.51072 \cdot 10^4$	99.5746
40.262	64.53952	0.4254
Totals	$1.51717 \cdot 10^4$

HPLC: CHIRALCEL OD 90/10 hexane / *iso*-propanol, 0.75 mL

Retention Times	Area	Area Percent
35.333	7371.13086	99.3480
40.812	48.37500	0.6520
Totals	7419.50586

HPLC: CHIRALCEL OD 90/10 hexane / *iso*-propanol, 0.75 mL

Retention Times	Area	Area Percent
32.021	$2.49689 \cdot 10^4$	98.2713
42.156	439.22418	1.7287
Totals	$2.54081 \cdot 10^4$

HPLC: CHIRALPAK OB-H 70/30 hexane / *iso*-propanol, 0.75 mL

Retention Times	Area	Area Percent
45.371	86.8483	1.2703
52.315	6749.92480	98.7297
Totals	6836.77324

HPLC: CHIRALPAK AD-H 80/20 hexane / *iso*-propanol, 0.75 mL

Retention Times	Area	Area Percent
26.273	$1.05435 \cdot 10^4$	99.7414
35.561	27.33446	0.2586
Totals	$1.05709 \cdot 10^4$

HPLC: CHIRALPAK AD-H 80/20 hexane / *iso*-propanol, 0.75 mL

Retention Times	Area	Area Percent
22.056	3631.35	99.853
31.810	5.3565	0.147
Totals	3636.70714	

¹H NMR Spectra