Practical Synthesis of Enantiopure Cyclic 1,2-Amino Alcohols via Catalytic Asymmetric Ring Opening of Meso Epoxides

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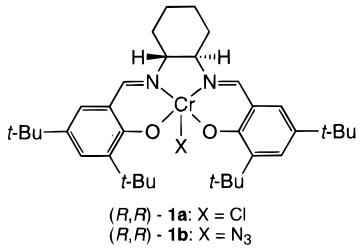
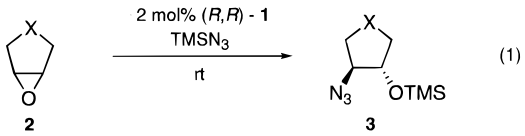
Introduction

The importance of cyclic 1,2-amino alcohols is evident from their presence in a wide variety of biologically important molecules[1] and in their successful application as stereochemical control elements.[2] The asymmetric ring opening (ARO) of meso epoxides with $TMSN_3$ catalyzed by chiral (salen)Cr(III) complexes (eq 1) provides efficient access to important representatives of this class of compounds from inexpensive, commercially available starting materials.[3] This paper provides a detailed description of the synthesis of a series of valuable cyclic *trans*- and *cis*-1,2-amino alcohols in optically pure form using the ARO methodology.[4]



(*R*,*R*) - **1a**: X = Cl
(*R*,*R*) - **1b**: X = N_3



2 **3** (1)

The (salen)Cr(III)Cl complex **1a** effectively catalyzes the ARO of various five- and six-membered ring-fused meso epoxides (Table 1, method A). The reactions can be run in the absence of solvent, and the ring-opened products are conveniently isolated by vacuum distillation of the reaction mixture. The nonvolatile residue recovered after distillation has been characterized as azide complex **1b**,[5] and this catalyst can be reused repeatedly in ARO reactions (method B) without loss of catalyst activity or enantioselectivity. In addition, complex **1b** catalyzes the formation of azido silyl ether product with no detectable byproducts[6] and, in certain cases, with measurably higher enantioselectivity than does **1a** (Table 1).[7]

Table 1. Asymmetric Ring Opening of 2a-d with $TMSN_3$ Catalyzed by (*R*,*R*)-1[a]

		% ee (%yield)[b]	
entry	X	method A[c]	method B[d]
a	CH_2	93 (97)	94 (99)
b	$(CH_2)_2$	85 (96)	88 (99)
c	O	97 (96)	97 (99)
d	$NCOCF_3$	95 (87)	95 (96)

[a] All reactions were run neat on 25−50 mmol of epoxide at rt using 1−2 mol % (*R*,*R*)-**1**, and the products were distilled from the catalyst under reduced pressure. [b] Yield based on mass recovery and corrected for purity, as determined by GC. [c] Method A refers to reactions with complex **1a**. [d] Method B refers to reactions with recycled complex **1b**.

Results and Discussion

The fact that the ARO displays a second-order dependence on catalyst concentration[8] has a negative practical consequence, as it limits to what extent catalyst loadings can be decreased before the reaction rates become impractically slow (e.g., a catalyst loading decrease of a factor of 10 leads to a 100-fold rate decrease). In this context, the catalyst recycling procedure is especially valuable, as it allows the production of multigram quantities of enantiomerically enriched ring-opened products **3a**−**d** from small amounts of catalyst (see Experimental Section).

The synthesis of the enantiomerically pure *trans*-amino alcohols **4a**−**c** was effected through a straightforward deprotection/reduction/recrystallization sequence (Scheme 1). Removal of the trimethylsilyl group was accomplished in MeOH using a catalytic amount of TFA (0.1 mol %) at room temperature. Reduction of the azide by addition of 2 mol % PtO_2 to the resulting methanolic solution and hydrogenolysis under balloon pressure at room temperature yielded the *trans*-amino alcohols in essentially quantitative yields. The crude products obtained by filtration from the hydrogenation catalyst and solvent evaporation were recrystallized to chemical and enantiomeric purity (>99% ee) with excellent product recovery. A survey of other hydrogenation catalysts revealed that 10% Pd/C was also effective at catalyzing the reduction of azide, but the product obtained required extensive purification resulting in lower yields. The one-pot two-step procedure employing PtO_2 thus proved to be the most effective and operationally-simple method for the production of gram quantities of enantiomerically enriched *trans*-amino alcohols.

The corresponding *cis*-amino alcohols **5a**−**c** were prepared from the hydroxy acetamides derived from **4a**−**c** by inversion of the hydroxyl group (Scheme 1). Oxazoline

(1) See, for example: (a) Wang, R.; Wong, C.-H. *Tetrahedron Lett.* **1996**, *37*, 5427. (b) Vacca, J. *et al. Proc. Natl. Acad. Sci. U.S.A.* **1994**, *91*, 4096. (c) Kikelj, D.; Kidric, J.; Pristovsek, P.; Pecar, S.; Urleb, U.; Krbavcic, A.; Hönig, H. *Tetrahedron* **1992**, *48*, 5915. (d) Shioiri, Y.; Hamada, Y. *Heterocycles* **1988**, *27*, 1035.

(2) (a) For a recent review: Ager, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 8350. (b) Davies, I. W.; Senanayake, C. H.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J. *Tetrahedron Lett.* **1996**, *37*, 1725.

(3) Martínez, L. E.; Leighton, J. L.; Carsten, D. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5897.

(4) For alternative synthetic approaches, see: (a) Börner, A.; Holz, J.; Kagan, H. B. *Tetrahedron Lett.* **1993**, *34*, 5273. (b) Barr, A. A.; Frencel, I.; Robinson, J. B. *Can. J. Chem.* **1977**, *55*, 4180. (c) Tamao, K.; Nakagawa, Y.; Ito, Y. *J. Org. Chem.* **1990**, *55*, 3438. (d) Seebach, D.; Eberle, M. *Chimia* **1986**, *40*. 315. (e) Fülöp, F.; Pihlaja, K.; Neuvonen, K.; Bernáth, G.; Argay, G.; Kálmán, A. *J. Org. Chem.* **1993**, *58*, 1967. (f) Didier, E.; Loubinoux, B.; Ramos Tombo, G. M.; Rihs, G. *Tetrahedron* **1991**, *47*, 4941. (g) Fischer *J. Org. Chem.* **1995**, *60*, 2026.

(5) Leighton, J. L.; Jacobsen, E. N. *J. Org. Chem.* **1996**, *61*, 389. This paper also describes the synthesis of complex **1b** directly from **1a** by metathesis of the chloride ligand.

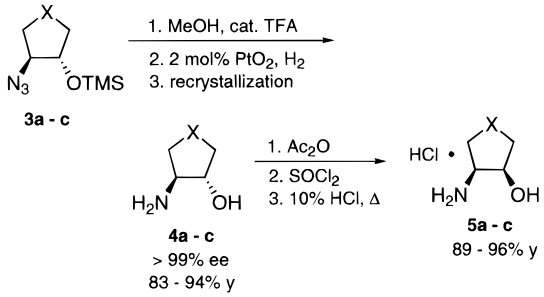
(6) As noted previously (ref 3), reactions employing catalyst **1a** produce detectable amounts ring-opened byproducts resulting from chloride transfer, at levels commensurate with the amount of catalyst used.

(7) **CAUTION!** Although these experiments have proceeded without incident, extreme caution should be excercised in the handling of organic and metal azides, particularly with manipulations that involve heating of neat liquids or solid residues.

(8) Hansen, K. B.; Leighton, J. L.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1996**, *118*, 10924.

S0022-3263(97)00146-1 CCC: $14.00

Scheme 1



formation with attendant inversion at the oxygen-bearing stereocenter was accomplished by activation of the hydroxy group with $SOCl_2$.[9] The oxazolines thus obtained were effectively pure by ^{1}H NMR analysis, and conversion to the pure *cis*-amino alcohols occurred upon heating the crude oxazoline salt to reflux in 10% HCl for 1 h followed by recrystallization of the hydrochloride salt.

Synthesis of pyrroline-derived 3,4-amino alcohols **6** and **7** was accomplished using a route similar to the one outlined above, although circumventing the use of acidic conditions (Scheme 2). Removal of the trimethylsilyl and trifluoroacetyl groups with basic methanol, followed by selective *N*-protection with di-*tert*-butyl dicarbonate afforded the corresponding Boc-protected azido alcohol. Reduction under H_2 catalyzed by PtO_2 yielded the *trans*-amino alcohol **6**, which was recrystallized to >99% ee in 85% overall yield from **3d**. Acylation with TFAA followed by mesylation and base-induced ring closure generated the 2-trifluoromethyl oxazoline.[10] Hydrolysis with K_2CO_3 in aqueous methanol yielded the *cis*-amino alcohol **7** in 92% yield.

The ARO of meso epoxides with $TMSN_3$ catalyzed by (*R*,*R*)-**1** thus provides a most sensible route to an assortment of useful *trans*- and *cis*-amino alcohols in optically pure form. The high volumetric productivity and ease of product isolation, as well as the possibility of recycling the catalyst with no loss of catalytic activity, render the ARO approach extremely attractive for the synthesis of amino alcohols on either laboratory or industrial scale.

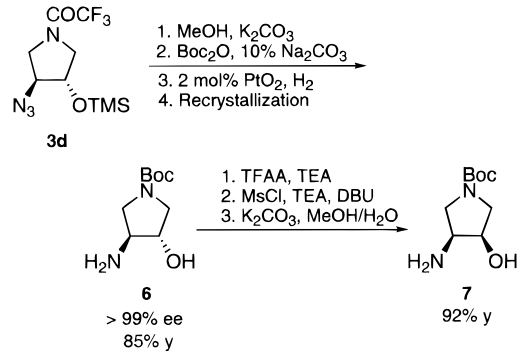
Experimental Section

Representative Procedure for the Asymmetric Ring Opening of Meso Epoxides with $TMSN_3$: Method A. (1*S*,2*S*)-2-Azido-1-(trimethylsiloxy)cyclopentane (3a). A 100 mL flask equipped with a stirbar was charged with 632 mg of (*R*,*R*)-**1a** (1.00 mmol, 0.02 equiv), flushed with N_2, and sealed. Cyclopentene oxide (4.40 mL, 50.0 mmol) and $TMSN_3$ (6.90 mL, 52.5 mmol, 1.05 equiv) were added sequentially at rt. The reaction mixture was allowed to stir 12 h, at which time the excess $TMSN_3$ was removed under reduced pressure, and the product **3a** was isolated by vacuum distillation (<0.5 mmHg, 40 °C) to afford a clear white oil (9.90 g, 49.7 mmol, 99%) which was shown to be 98% pure by GC and in 93% ee by chiral GC analysis.

Method B. The flask containing catalyst from method A was flushed with N_2 and then charged with cyclopentene oxide (8.80 mL, 100 mmol) and $TMSN_3$ (13.8 mL, 105 mmol). The reaction was allowed to stir at rt for 24 h at which time the remaining $TMSN_3$ was removed in vacuo, and the product was isolated by vacuum distillation to provide **3a** (19.8 g, 99.3 mmol, 99%) in 94% ee by chiral GC analysis.

(1*S*,2*S*)-2-Azido-1-(trimethylsiloxy)cyclohexane (3b). Method A. The product was isolated by distillation (<0.5 mmHg, 50 °C) as a clear white oil (10.6 g, 49.5 mmol, 99%), 97% pure by GC and 85% ee by chiral GC analysis. **Method B.** The ARO was carried out using catalyst **1b** recovered from method A and 50 mmol of cyclohexene oxide. Yield from **2b**: 10.6 g, 49.8 mmol, 99%; 87% ee.

Scheme 2



(3*S*,4*S*)-4-Azido-3-(trimethylsiloxy)tetrahydrofuran (3c). Method A. The product was isolated by distillation (<0.5 mmHg, 45 °C) as a clear white oil (9.95 g, 49.5 mmol, 99%), 97% pure by GC and 97% ee by chiral GC analysis. **Method B.** Yield from **2c** (50 mmol): 10.0 g, 49.7 mmol, 99%; 97% ee.

(3*S*,4*S*)-4-Azido-3-(trimethylsiloxy)-1-(2,2,2-trifluoroacetyl)pyrrolidine (3d). Method A. The product was isolated by distillation (<0.5 mmHg, 90 °C) as a clear white oil (13.5 g, 45.6 mmol, 91%) which was shown to be 96% pure by GC and 95% ee by chiral GC analysis. **Method B.** Yield from **2d** (50 mmol): 14.2 g, 48.0 mmol, 96%; 95% ee.

General Procedure for the Synthesis of *trans*-Amino Alcohols from 3: (1*S*,2*S*)-2-Aminocyclopentanol (4a). A 1 L flask equipped with a stirbar was charged with **3a** (20.3 g, 102 mmol), MeOH (340 mL, 0.3 M), and TFA (7 μL, 0.09 mmol), and the mixture was allowed to stir at rt for 30 min. The resulting solution was treated with solid PtO_2 (432 mg, 1.90 mmol) and placed under a H_2 atmosphere (balloon pressure) and stirred for 40 h at rt. The solution obtained by filtration through Celite and washing the filter cake with MeOH was concentrated in vacuo to produce a clear tan-colored solid. This material was dissolved in 30 mL of hot toluene, and the volume of the solution was reduced under reduced pressure to 30 mL and then cooled to 4 °C. The resulting crystals were separated from the mother liquor and rinsed with cold toluene. The recrystallization procedure was repeated twice to yield amino alcohol **4a** in >99% ee (determined by chiral GC analysis of the *N*,*O*-bis-trifluoroacetyl derivative obtained by treatment of the amino alcohol with TFAA [Chiraldex γ-TA (20 m × 0.25 mm i.d. × 0.125 μm film), Advanced Separation Technologies, Inc., Whippany, NJ, cat. no. 71020, 100 °C isothermal]. Due to its hygroscopic nature, the amino alcohol was converted to the HCl salt for the purposes of characterization. Crystalline **4a** was dissolved in 10 mL of EtOH and diluted to 250 mL with Et_2O. Gaseous HCl was bubbled through until no more precipitate was formed. The mixture was filtered and the off-white solid collected to yield 12.8 g (93 mmol, 91%). $[\alpha]^{26}_D$ +29.7 (*c* 1.95, EtOH); ^{1}H NMR (CD_3OD, 400 MHz) δ 4.04 (dd, 1H, J = 6.6 and 13.0 Hz), 3.24 (dd, 1H, J = 6.2 and 8.0 Hz), 2.13−2.18 (m, 1H), 1.99−2.02 (m, 1H), 1.75−1.83 (m, 2H), 1.55−1.65 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ 76.7, 59.7, 33.3, 28.8, 21.1. HRMS calcd for $C_5H_{15}N_2O$ $(M + NH_4)^+$: 119.1184. Found: 119.1188.

(1*S*,2*S*)-2-Aminocyclohexanol (4b). The crude solid product obtained from the hydrogenation reaction was dissolved in 60 mL of hot toluene, and the solution was cooled to 4 °C. The mother liquor was decanted, and the resulting crystals were rinsed with cold toluene. The recrystallization procedure was repeated, and the solid was collected by filtration to yield the amino alcohol in >99% ee (determined by chiral HPLC analysis of the 2,4-dinitroaniline product obtained by reaction with Sanger's reagent, [Chiralcel OD (250 cm × 4.6 mm i.d.), Chiral Technologies, Inc., 1.0 mL/min, 75:25 hexanes:IPA]. The amino alcohol was converted to its HCl salt (9.40 g, 81.6 mmol, 83%) for the purposes of characterization and storage. **4b·HCl**: Opaque white solid. $[\alpha]^{26}_D$ +37.0 (*c* 1.10, EtOH); ^{1}H NMR (CD_3OD, 400 MHz) δ 3.36−3.41 (m, 1H), 2.79−2.85 (m, 1H), 2.01−2.04 (m, 2H), 1.76−1.78 (m, 2H), 1.30−1.40 (m, 4H); ^{13}C NMR (CD_3OD, 100 MHz) δ 72.4, 57.7, 35.2, 30.3, 25.13, 25.08. HRMS calcd for $C_6H_{14}NO$ $(M + H)^+$: 116.1075. Found: 116.1079.

(9) Bannard, R. A. B.; Gibson, N. C. C.; Parkkari, J. H. *Can. J. Chem.* **1971**, *49*, 2064.

(10) Golding, B. T.; Nassereddin, I. K. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2017.

(3*S*,4*S*)-4-Amino-3-hydroxytetrahydrofuran (4c). The crude solid product obtained from the hydrogenation reaction was dissolved in 10 mL of hot EtOH, and the solution was diluted with 15 mL of Et_2O and cooled to 4 °C. The mother liquor was decanted, and the resulting crystals were rinsed with cold Et_2O. Chiral GC analysis of the *N*,*O*-bis-trifluoroacetyl derivative indicated that the amino alcohol was present in >99% ee (γ-TA, 120 °C isothermal). The HCl salt was generated as described above: 12.8 g (93 mmol, 91%). $[\alpha]^{26}_D$ +16.9 (*c* 1.79, EtOH); ^{1}H NMR (CD_3OD, 400 MHz) δ 4.33 (s, br, 1H), 4.14 (dd, 1H, J = 5.4 and 10.0 Hz), 4.01 (dd, 1H, J = 4.9 and 10.5 Hz), 3.80 (d, 1H, J = 10.5 Hz), 3.59−3.63 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ 75.2, 75.0, 70.3, 59.6. HRMS calcd for $C_4H_{13}N_2O_2$ $(M + NH_4)^+$: 121.0977. Found: 121.0979.

General Procedure for the Synthesis of *cis*-Amino Alcohols from 4: (1*R*,2*S*)-2-Aminocyclopentanol Hydrochloride (5a). A 250 mL flask equipped with a stir bar was charged with 4.82 g (35.2 mmol) of the HCl salt of **4a**. The material was suspended in 35 mL of acetone and cooled to 0 °C. The rapidly-stirred mixture was treated with 35 mL of aqueous 10% Na_2CO_3 followed by slow addition of Ac_2O (3.33 mL, 35.2 mmoL). The reaction was allowed to warm to rt over 1 h and stirred for an additional 2 h, during which time the solution became homogeneous. The reaction was diluted with 10 mL each of $NaHCO_3$ (saturated) and NaCl (saturated). The solution was then extracted 5 × 9:1 $CHCl_3$:IPA. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated to yield 4.75 g (33.3 mmol, 95%) of the crude hydroxy acetamide as a viscous oil. This material was dissolved in 17 mL of $CHCl_3$ and slowly added to neat $SOCl_2$ with stirring (10.2 mL, 141 mmol) at 0 °C. The reaction was allowed to warm to rt over 1 hour and stirred for an additional 2 h. The crude mixture was concentrated *in vacuo* to yield the cis-fused bicyclic oxazoline·HCl salt. Analysis of the ^{1}H NMR spectrum of the crude product indicated clean conversion to the oxazoline salt (see Supporting Information), so this material was used without further purification. The material was dissolved in 117 mL of aqueous 10% HCl and heated to reflux for 1 h. The cooled solution was concentrated *in vacuo*, and the resulting residue was dissolved in 1:1 MeOH:CH_2Cl_2. The mixture was filtered through Celite, and the filtrate was concentrated to yield off-white crystals which were recrystallized from EtOH/Et_2O to afford 4.30 g (31.2 mmol, 89%) of opaque white crystals of **5a·HCl**. $[\alpha]^{26}_D$ −18.6 (*c* 1.14, EtOH); ^{1}H NMR (CD_3OD, 400 MHz) δ 4.21 (dd, 1H, J = 4.1 and 8.2 Hz), 3.40 (dd, 1H, J = 7.9 and 13.0 Hz), 2.01−2.05 (m, 1H), 1.88−1.94 (m, 2H), 1.64−1.75 (m, 3H); ^{13}C NMR (CD_3OD, 100 MHz) δ 71.8, 55.6, 33.7, 28.5, 21.3. HRMS calcd for $C_5H_{15}N_2O$ $(M + NH_4)^+$: 119.1184. Found: 119.1185.

(1*R*,2*S*)-2-Aminohexanol Hydrochloride (5b). The solid obtained from hydrolysis of the oxazoline was recrystallized from EtOH/Et_2O to yield 4.24 g (28.0 mmol, 93%) of opaque white crystals. $[\alpha]^{26}_D$ −27.9 (*c* 1.10, EtOH); ^{1}H NMR (CD_3OD, 400 MHz) δ 3.95−3.96 (m, 1H), 3.29−3.31 (m, 1H), 1.57−1.79 (m, 6H), 1.39−1.42 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ 66.5, 54.0, 32.3, 26.1, 24.2, 20.1. HRMS calcd for $C_6H_{13}NO$ $(M)^+$: 115.0997. Found: 115.0997.

(3*R*,4*S*)-4-Amino-3-hydroxytetrahydrofuran Hydrochloride (5c). A 250 mL flask was charged with **4c** (3.03 g, 29.5 mmol), capped with a rubber septum, placed under N_2 atmosphere, and cooled to 0 °C. The material was suspended in 30 mL of CH_2Cl_2, and then Ac_2O (8.40 mL, 88.5 mmol) was added by syringe. The reaction was allowed to warm to rt over 1 hour at which time the reaction became homogenous. The reaction was allowed to stir at room temperature for 1 h, and then solvent was removed *in vacuo* to yield the crude acetamide as an off-white solid. This material was converted to the crude *cis*-amino alcohol **5c**·HCl according to the general procedure. The crude material was dissolved in 10 mL of hot EtOH and diluted with 20 mL of THF. The mixture was heated until dissolution was complete and then cooled to 4 °C. After 18 h, the resulting opaque white platelets were collected by vacuum filtration to yield **5c**·HCl (3.95 g, 28.3 mmol, 96%). $[\alpha]^{26}_D$ −2.6 (*c* 1.03, EtOH); ^{1}H NMR (CD_3OD, 400 MHz) δ 4.50 (dd, 1H, J = 5.2 and 8.4 Hz), 3.91−3.99 (m, 2H), 3.72−3.82 (m, 3H); ^{13}C NMR (CD_3OD, 100 MHz) δ 75.3, 70.2, 70.1, 54.0. HRMS calcd for $C_4H_{10}NO_2$ $(M + H)^+$: 104.0712. Found: 104.0713.

(3*S*,4*S*)-4-Amino-3-hydroxy-1-(*tert*-butoxycarbonyl)pyrrolidine (6). A 1 L flask equipped with a stirbar was charged with **3d** (17.01 g, 57.4 mmol). The material was dissolved in 570 mL of MeOH (0.1 M) and treated with solid K_2CO_3 (7.93 g, 57.4 mmol). The mixture was allowed to stir at rt for 5 h solvent was removed *in vacuo*, and the residue was dissolved in 60 mL of 10% Na_2CO_3 and 60 mL of acetone. The solution was cooled to 0 °C and treated with 13.2 mL (57.4 mmol) of di-*tert*-butyl dicarbonate. The reaction was allowed to warm to rt and stirred for 12 h. The resulting mixture was diluted with H_2O and extracted with $CHCl_3$ (3×). The combined extracts were dried over Na_2SO_4 and concentrated, and the residue was purified by chromatography over SiO_2 using 9:1 to 3:1 hexanes:acetone as the eluent. The clear white oil obtained was dissolved in 190 mL of MeOH and treated with 255 mg (1.12 mmol) of PtO_2. The reaction was placed under H_2 (balloon pressure) and stirred 26 h at rt. The mixture was filtered through Celite, and the filter cake was rinsed with MeOH. Concentration of the filtrate provided crude **6** as an opaque white solid. This material was dissolved in 200 mL of boiling CH_2Cl_2. The volume was concentrated to 120 mL, and the solution was allowed to cool to 4 °C. The solid was collected by filtration to yield **6** (9.86 g, 48.7 mmol, 85%) in >99% ee (chiral HPLC analysis of the product obtained by reaction with Sanger's reagent, Pirkle Covalent S-N1N-Naphthylleucine column, 0.60 mL/min, 96:4 hexanes:IPA for 57 min to 95:5 from 59−80 min). $[\alpha]^{26}_D$ −2.3 (*c* 1.03, EtOH); ^{1}H NMR (CD_3OD, 400 MHz) δ 3.94 (s(br), 1H), 3.56−3.60 (m, 2H), 3.12−3.24 (m, 3H), 1.45 (s, 9H); ^{13}C NMR (CD_3OD, 100 MHz) δ 156.6, 80.9, 77.0, 76.4, 58.4, 57.8, 52.9, 52.6, 52.4, 52.2, 29.1. HRMS calcd for $C_9H_{19}N_2O_3$ $(M + H)^+$: 203.1396. Found: 203.1395.

(3*R*,4*S*)-4-Amino-3-hydroxy-1-(*tert*-butoxycarbonyl)pyrrolidine (7). A 250 mL oven-dried flask was charged with **6** (4.34 g, 21.5 mmol) and a stir bar, sealed with a rubber septum, and placed under N_2. The material was suspended in 70 mL of THF (0.3 M) and cooled to 0 °C, and TFAA (3.03 mL, 21.5 mmol) and TEA (3.60 mL, 25.8 mmol) were added sequentially. The reaction was allowed to warm to rt and stirred 12 h at which time the solution was diluted with H_2O and extracted 3 × 9:1 $CHCl_3$:IPA. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude trifluoroacetamide thus obtained was dissolved in 110 mL of CH_2Cl_2 (0.2 M) and cooled to 0 °C under N_2, followed by addition of TEA (3.6 mL, 25.8 mmol) and MsCl (1.48 mL, 23.6 mmol). The reaction was allowed to stir 15 min at 0 °C and then at rt for 1 h. Oxazoline formation was affected by treatment of the reaction mixture with DBU (9.64 mL, 64.5 mmol). Stirring was continued for 30 min at which time the reaction mixture was concentrated under reduced pressure, filtered through SiO_2, and rinsed with 300 mL of 3:2 hexanes:acetone. The filtrate was concentrated, and the crude oil was dissolved in 80 mL of MeOH and 40 mL of H_2O. Hydrolysis was effected by addition of solid K_2CO_3 (18.0 g, 129 mmol). The reaction was allowed to stir for 10 h at which time the volume was reduced *in vacuo*. The aqueous layer was extracted 5 × 9:1 $CHCl_3$:IPA, and the combined extracts were dried over K_2CO_3. The extracts were filtered and concentrated to yield a crude solid which was recrystallized from CH_2Cl_2 to yield **7** (3.98 g, 19.7 mmol, 92%) as opaque white platelets. $[\alpha]^{26}_D$ +5.0 (*c* 1.08, EtOH); ^{1}H NMR (CD_3OD, 400 MHz) δ 4.04−4.06 (m, 1H), 3.51−3.56 (m, 1H), 3.44 (td, 1H, J = 4.4 and 12.1 Hz), 3.33 (m, 1H), 3.01 (t, 1H, J = 10.1 Hz), 1.45 (s, 9H); ^{13}C NMR (CD_3OD, 100 MHz) δ 156.4, 80.92, 80.86, 72.3, 71.6, 55.0, 54.5, 54.0, 53.7, 51.3, 50.9, 28.7. HRMS calcd for $C_9H_{19}N_2O_3$ $(M + H)^+$: 203.1396. Found: 203.1391.

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Supporting Information Available: Chromatographic analyses of racemic and enantiomerically pure *trans*-amino alcohol derivatives, and copies of ^{1}H NMR spectra of all relevant synthetic intermediates and products (25 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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