Gold(I)-Catalyzed Asymmetric Aldol Reaction of *N*-Methoxy-*N*-methyl-α-isocyanoacetamide (α-Isocyano Weinreb Amide). An Efficient Synthesis of Optically Active β-Hydroxy α-Amino Aldehydes and Ketones

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Asymmetric aldol reaction of *N*-methoxy-*N*-methyl-α-isocyanoacetamide (α-isocyano Weinreb amide) with aldehydes [RCHO: R = Ph, Me, *i*-Pr, (*E*)-MeCH=CH, (*E*)-BnOCH$_2$CH=CH] in the presence of a gold(I) catalyst prepared *in situ* from [Au(*c*-HexNC)$_2$]BF$_4$ and chiral ferrocenylphosphine ligand (*R*)-*N*-methyl-*N*-(2-morpholinoethyl)-1-[(*S*)-1′,2-bis(diphenylphosphino)ferrocenyl]ethylamine gave high yields of optically active *trans*-5-alkyl-2-oxazoline-4-(*N*-methoxy-*N*-methylcarboxamides) with high diastereo- and enantioselectivities. The diastereoselectivities (trans:cis) and enantiomeric excesses of the *trans*-oxazolines for the reaction with 1 mol % of the catalyst are as follows: R = Ph, 97:3, 96% ee; R = Me, 95:5, 97% ee; R = *i*-Pr, 98:2, 97% ee; R = (*E*)-MeCH=CH, 97:3; 99% ee; (*E*)-BnOCH$_2$CH=CH, 96:4, 95% ee. These optically active oxazolines were converted to *N*,*O*-protected β-hydroxy-α-amino aldehydes and ketone in high yields. An *N*-protected α-amino aldehyde (R = Ph) lacking the β-hydroxyl group was also obtained through the catalytic hydrogenolysis of the oxazoline.

Introduction

Optically active α-amino aldehydes[1,2] and ketones[3] are of great interest as chiral building blocks for the synthesis of polyfunctional unusual amino acids,[4] amino polyols such as amino sugars,[5] and peptide mimics such as enzyme inhibitors.[6–9] These compounds are usually synthesized through transformations of natural common α-amino acids. Since the structures of amino acid side chains available from this methodology are restricted, the development of the asymmetric synthesis of α-amino aldehydes with unnatural side chain structures is highly desirable.

N-Protected α-amino aldehydes can be prepared by oxidation of *N*-protected amino alcohols or by reduction of amino acids or their esters with DIBALH.[2a] However, the most efficient and reliable method for the preparation of the aldehydes is probably the reduction of Weinreb amides (*N*-methoxy-*N*-methylamides) of *N*-protected amino acids with LiAlH$_4$ or DIBALH.[2b,c,10] On the other hand, we have been studying the asymmetric aldol reaction of isocyano carboxylates and their derivatives with aldehydes catalyzed by gold(I) complexes coordinated with optically active ferrocenylphosphine ligands (**1**) bearing pendant 2-(dialkylamino)ethylamino groups, which provides an efficient route to optically active β-hydroxy α-amino acids (Scheme 1).[11,12] The high efficiency of these gold catalysts has been explained by a previously proposed transition state as in structure **A**, where the terminal amino group in **1** abstracts one of the active methylene hydrogens of the gold-coordinated isocyanoacetate derivative, forming an ion pair between the enolate anion and the ammonium cation. This attractive interaction (*secondary ligand–substrate interaction*[12b]) permits a favorable arrangement of the enolate and the aldehyde

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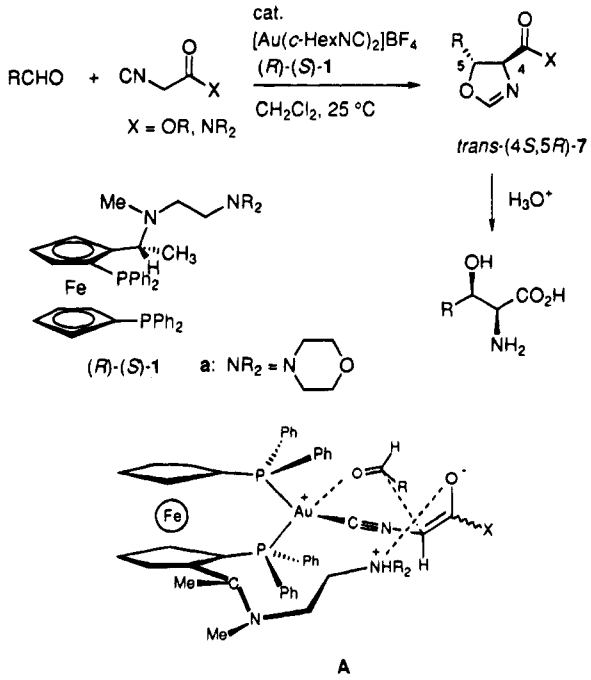
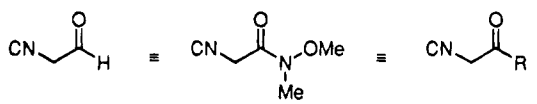
Scheme 1



on the gold in the stereodifferentiating transition state. The aldol adduct thus formed cyclizes immediately to form an oxazoline, which no longer coordinates to the gold, being replaced by the starting isocyanoacetate.

With the established usefulness and versatility of Weinreb amides in mind,[9c,d,13] we have synthesized *N*-methoxy-*N*-methyl-α-isocyanoacetamide (α-isocyano Weinreb amide, **2**), which is synthetically equivalent to isocyanoacetaldehydes and isocyanomethyl alkyl ketones, and applied it to the gold-catalyzed asymmetric aldol reaction. In this paper we wish to report an efficient synthesis of optically active *N,O*-protected β-hydroxy α-amino aldehydes and ketone and *N*-protected α-amino aldehyde lacking β-hydroxyl group through the highly stereoselective gold-catalyzed asymmetric aldol reaction of the α-isocyano Weinreb amide with aldehydes.



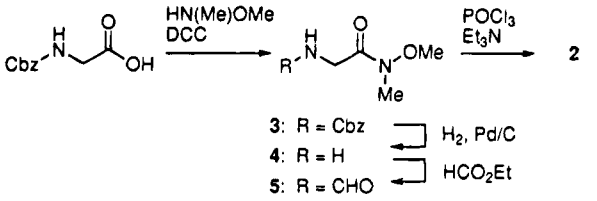
2

α-Isocyano Weinreb Amide

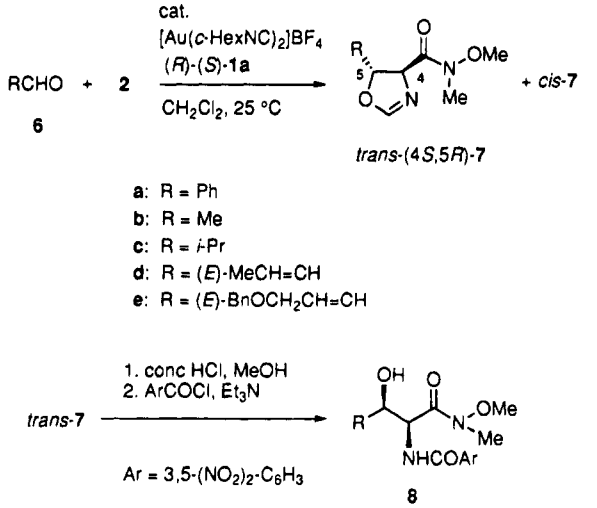
Results and Discussion

Synthesis of α-Isocyano Weinreb Amide. The synthesis of α-isocyano Weinreb amide **2** is shown in Scheme 2. *N*-(Carbobenzyloxy)glycine was coupled with *N,O*-dimethylhydroxylamine to give amide **3**, the carbobenzyloxy group was removed by hydrogenolysis, and then the amino group of **4** was formylated. Dehydration of the formamide **5** with $POCl_3$ gave α-isocyano Weinreb amide **2** as crystals. An alternative route for the synthesis of the amide **2** by the reaction of methyl isocyanoacetate with *N,O*-dimethylhydroxylamine in refluxing methanol was examined. This condensation reaction,

Scheme 2



Scheme 3



however, resulted in low conversion of the starting materials. Therefore, the former synthetic route was adopted for a large scale preparation.

Gold(I)-Catalyzed Asymmetric Aldol Reaction of α-Isocyano Weinreb Amide. The aldol reaction of α-isocyano Weinreb amide **2** with aldehydes **6a–e** was carried out in essentially the same manner as that of isocyanoacetate (Scheme 3). The reaction conditions and results are summarized in Table 1. A typical procedure using 1 mol % of catalyst is given for the reaction of benzaldehyde (**6a**). To a solution of 40.5 mg (0.056 mmol) of chiral ferrocenylphosphine [(*R*)-(*S*)-**1a**], 25.0 mg (0.050 mmol) of bis(cyclohexyl isocyanide)gold(I) tetrafluoroborate, and 0.641 g (5.00 mol) of **2** in 2.5 mL of CH_2Cl_2 was added 0.695 g (6.55 mmol) of **6a** at room temperature. The mixture was then stirred at 25 °C for 20 h. The ^1H NMR of an aliquot indicated that 5-phenyl-2-oxazoline-4-(*N*-methoxy-*N*-methylcarboxamide) (**7a**) was produced quantitatively with a trans:cis ratio of 97:3. Chromatography on silica gel gave 1.012 g (86%) of analytically pure *trans*-(4*S*,5*R*)-**7a**. The enantiomeric excess was determined to be 96% by HPLC analysis of its 3,5-dinitrobenzamide derivative **8a** with a chiral stationary phase column (Sumichiral OA-4500). With 0.2 mol % of the gold catalyst, the reaction of **6a** still proceeded smoothly at 25 °C and was completed within 45 h in high stereoselectivities; trans:cis = 97:3, 93% ee.

High levels of diastereoselectivities (trans:cis) and enantioselectivities were also observed for the aldol reaction of saturated aliphatic aldehydes such as acetaldehyde (**6b**, 94:6, 97% ee for *trans*-**7b**) and isobutyraldehyde (**6c**, 98:2, 97% ee for *trans*-**7c**). The reaction of α,β-unsaturated aldehydes such as crotonaldehyde (**6d**) and (*E*)-4-(benzyloxy)-2-butenal (**6e**) proceeded without the formation of conjugate addition products, giving 5-(1-alkenyl)-2-oxazoline-4-carboxamides (**7d,e**) with high stereoselectivities: 97:3, 99% ee for *trans*-**7d**; 96:4, 95% ee for *trans*-**7e**. The oxazolines derived from α,β-

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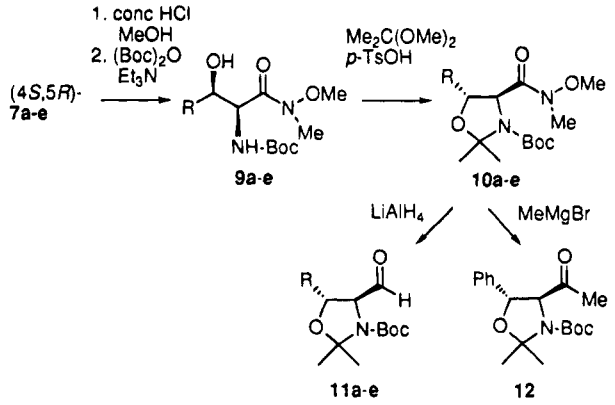
Table 1. Asymmetric Aldol Reaction of *N*-Methoxy-*N*-methyl-α-isocyanoacetamide (2) with Aldehydes 6 Catalyzed by Chiral Ferrocenylphosphine–Gold(I) Complex (Scheme 3)[a]

aldehyde (6)	ratio of [2]:[cat]	time, h	ratio of trans:cis	*trans*-7 yield,[b] %	*trans*-7 ee,[c] % (confign)
PhCHO (**6a**)	100:1	20	97:3	86 (**7a**)	96 (4*S*,5*R*)[e]
PhCHO (**6a**)	500:1	45	97:3	84 (**7a**)	93 (4*S*,5*R*)[f]
MeCHO (**6b**)	100:1	15	95:5	*d* (**7b**)	97 (4*S*,5*R*)[g]
i-PrCHO (**6c**)	100:1	17	98:2	90 (**7c**)	97 (4*S*,5*R*)[g]
(*E*)-MeCH=CHCHO (**6d**)	100:1	37	97:3	94 (**7d**)	99 (4*S*,5*R*)[g]
(*E*)-BnOCH$_2$CH=CHCHO (**6e**)	100:1	48	96:4	82 (**7e**)	95 (4*S*,5*R*)[g]

[a] The reaction was carried out in CH_2Cl_2 at 25 °C. **2**:**6** = 1:1.2 for **6a**,**c**–**e**, 1:3.4 for **6b**. [b] Isolated yield by column chromatography on silica gel. [c] Determined by HPLC analysis of **8** with a chiral stationary phase column (Sumitomo Chemical Co., Sumichiral OA). OA 4100 for **7a** and OA-4500 for **7b**–**e**. [d] Crude mixture of *trans*-**7b** and *cis*-**7b** was used for further transformation. [e] Configuration determined by HPLC analysis of N^{α}-(3,5-dinitrobenzoyl)phenylalanine-*N*-methoxy-*N*-methylamide with Sumichiral OA-4100. Authentic samples were prepared with DL- and L-phenylalanine. [f] Configuration determined by the optical rotation of **11b** (ref 2e). [g] Configuration assigned by the similarity of its optical rotation with those of optically active *trans*-*N*,*N*-dialkyl-5-alkyl-2-oxazoline-4-carboxamides (Ito, Y.; Sawamura, M.; Kobayashi, M.; Hayashi, T. *Tetrahedron Lett.* **1988**, *29*, 6321).

Scheme 4



unsaturated aldehydes will be useful intermediates for the synthesis of highly functionalized compounds such as amino polyols, because those oxazolines bear an olefinic substituent which may be functionalized with stereoselective transformations such as epoxidation, dihydroxylation, halo lactonization, and some related intramolecular reactions. The diastereoselectivities and enantioselectivities have both been remarkably improved upon comparison with those for the reaction of isocyanoacetate, while the enantioselectivities for the reaction of benzaldehyde (**6a**) and the diastereoselectivity for that of isobutyraldehyde (**6c**) are comparable with the previous results.[14] For example, the diastereoselectivity and enantioselectivity for the reaction of methyl isocyanoacetate with (*E*)-2-hexenal and acetaldehyde (**6b**) have been 87:13, 92% ee and 89:11, 89% ee, respectively.

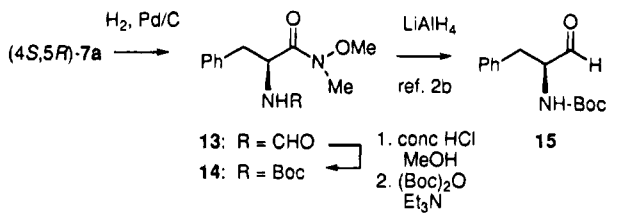
Synthesis of *N*,*O*-Protected β-Hydroxy α-Amino Aldehydes and Ketones. As shown in Scheme 4, optically active *trans*-oxazolines **7a**–**e** were converted into N^{α}-^{t}Boc-protected β-hydroxy-α-amino amides **9a**–**e** via β-hydroxy α-amino amides, and then the hydroxyl groups of **9** were protected as *N*,*O*-acetonides (**10a**–**e**). Of the various protecting groups for the β-hydroxyl group of **9**, *N*,*O*-acetonide was tentatively chosen for this study because it has been reported in the literature[2c] that optically active serinal and threoninal protected in this manner are chemically and configurationally stable enough to be isolated by chromatography on silica gel or by distillation. For the reduction of *N*-methoxy-*N*-methylamide groups of **10** leading to *N*,*O*-protected β-hydroxy α-amino aldehydes **11a**–**e**, the reported procedure[2b] for the reduction of Weinreb amides derived from natural amino acids was followed. Thus, Weinreb amides **10a**–**e** were treated with a 5-fold excess of $LiAlH_4$ (based on H) at 0 °C. The reaction was complete within 15 min according to the monitoring by TLC. After aqueous workup, quantitative yields of aldehydes **11a**–**e** were obtained. The ^{1}H NMR spectra indicated that these crude materials contained neither the starting amides, epimerization products, nor primary alcohols which could have been produced by an overreduction, and satisfactory data of elemental analyses (±<0.6% except **11e**) were obtained at this stage. Further purification by MPLC or bulb-to-bulb distillation gave **11** with higher purities in excellent yields. The yields of **9**–**11** are summarized in Table 2.

Table 2. Conversion of *trans*-Oxazolines 7 to Optically Active *N*,*O*-Protected β-Hydroxy-α-amino Aldehydes 11 (Scheme 4)

trans-(4*S*,5*R*)-**7**	**9** yield,[a] %	**10** yield,[b] %	**11** yield[c] (yield),[d] %
7a, R = Ph	92	89	96 (99)
7b, R = Me	*e*	71[f]	91 (97)
7c, R = *i*-Pr	88	86	95 (99)
7d, R = (*E*)-MeCH=CH	84	76	95 (98)
7e, R = (*E*)-BnOCH$_2$CH=CH	85	79	80 (96)

[a] Isolated yield based on *trans*-**7**. [b] Isolated yield based on **9**. [c] Isolated yield based on **10**. [d] Yield based on **10** after aqueous workup. [e] Not isolated. [f] Isolated yield based on **2**.

Scheme 5



Synthesis of *N*-Boc-L-phenylalaninal. As exemplified by the transformation of (4*S*,5*R*)-**7a** shown in Scheme 5, oxygen functionality at the β-position of oxazoline derived from aromatic aldehydes can be removed by means of catalytic hydrogenolysis of benzylic C–O bond.[15] The palladium-catalyzed hydrogenolysis of *trans*-**7a** (140 atm, rt, in EtOH) gave N^{α}-formyl-L-phenylalanine-*N*-

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(14) Schöllkopf, G. U.; Hoppe, D. *Angew. Chem.* **1970**, *82*, 483.

methoxy-*N*-methylamide (**13**) quantitatively, which was converted into N^{α}-*t*Boc-L-phenylalanine-*N*-methoxy-*N*-methylamide (**14**). The reduction of **14** with $LiAlH_4$ has already been reported to give *N*-*t*Boc-L-phenylalaninal (**15**) without racemization.[2b]

Experimental Section

Materials. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. CH_2Cl_2 for the aldol reaction was dried over CaH_2 and distilled under nitrogen atmosphere. THF and Et_2O for reaction solvents were distilled from sodium/benzophenone ketyl under nitrogen atmosphere. Bis(cyclohexyl isocyanide)-gold(I) tetrafluoroborate,[16] ferrocenylphosphine **1a**,[17] and aldehyde **6e**[18] were prepared according to the literature procedure.

***N*$^{\alpha}$-(Carbobenzyloxy)glycine-*N*-methoxy-*N*-methylamide (3).** To a solution of 45.06 g (0.738 mol) of *N*,*O*-dimethylhydroxylamine [distilled from a mixture of *N*,*O*-dimethylhydroxylamine hydrochloride, triethanolamine, and ethylene glycol (1:1.5:1.5, w:w:w)] in 1 L of CH_2Cl_2 were added 104.61 g (0.500 mol) of *N*-(carbobenzyloxy)glycine and 113.53 g (0.550 mol) of DCC in this order at 0 °C. The mixture was stirred at 0 °C for 5 h and at rt for 2 d and then refluxed for 12 h. The precipitate was filtered off and washed with CH_2Cl_2. The filtrate and washings were combined and evaporated. Recrystallization of the residual solid from EtOAc/CH_2Cl_2 gave 95.21 g (76%) of **3** as colorless crystals: mp 76−77 °C; ^{1}H NMR ($CDCl_3$) δ 3.21 (s, 3 H), 3.72 (s, 3 H), 4.14 (d, J = 4.4 Hz, 2 H), 5.13 (s, 2 H), 5.56 (br s, 1 H), 7.30−7.39 (m, 5 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 32.4, 42.1, 61.4, 66.9, 127.99, 128.04, 128.4, 136.4, 156.3, 169.7. Anal. Calcd for $C_{12}H_{16}N_2O_4$: C, 57.13; H, 6.39; N, 11.10. Found: C, 57.36; H, 6.42; N, 11.06.

Glycine-*N*-methoxy-*N*-methylamide (4). Under a hydrogen atmosphere, a solution of 92.1 g (0.369 mol) of **3** in 750 mL of MeOH was added to 7.88 g (3.7 mmol) of 5% Pd/C. The mixture was hydrogenated at atmospheric pressure for 65 h. Filtration and evaporation gave 37.3 g (86%) of crude **4** as an oil, which was used without further purification: ^{1}H NMR ($CDCl_3$) δ 3.21 (s, 3 H), 3.58 (s, 2 H), 3.69 (s, 3 H).

***N*$^{\alpha}$-Formylglycine-*N*-methoxy-*N*-methylamide (5).** A solution of 37.3 g (0.316 mmol) of **4** in 128 mL (1.58 mol) of ethyl formate was refluxed for 20 h. The resulting suspension was filtered, and the solid was washed with EtOAc. The filtrate and washings were combined and evaporated. EtOAc was added to the residue, and the precipitate was filtered off. Evaporation of the filtrate gave 34.1 g (74%) of **5** as a brown oil, which was used without further purification: ^{1}H NMR ($CDCl_3$) δ 3.24 (s, 3 H), 3.74 (s, 3 H), 4.25 (d, J = 4.7 Hz, 2 H), 6.57 (br s, 1 H), 8.27 (s, 1 H).

***N*-Methoxy-*N*-methyl-α-isocyanoacetamide (2).** To a solution of 34.1 g (0.233 mol) of **5** and 94.5 g (0.934 mol) of Et_3N in 470 mL of THF was added 37.5 g (0.247 mol) of $POCl_3$ over 20 min at 0 °C. The mixture was stirred at 0 °C for 2 h and at rt for 4 h. Saturated aqueous $NaHCO_3$ (ca 200 mL) and CH_2Cl_2 (ca 500 mL) were added at 0 °C and the resulting mixture stirred at rt for 15 min. The mixture was filtered through a pad of Celite, and the solid was washed with CH_2Cl_2. The filtrate and washings were combined and diluted with water. The organic phase was separated, and the aqueous phase was extracted six times with CH_2Cl_2. The combined organic phases were dried over K_2CO_3 and $MgSO_4$ and evaporated. Chromatography of the residue on silica gel (8 × 50 cm, hexane:EtOAc = 3:1−1:2) gave 15.1 g (50%) of **2** as colorless crystals: mp 82 °C; ^{1}H NMR ($CDCl_3$) δ 3.24 (s, 3 H), 3.73 (s, 3 H), 4.41 (s, 2 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 32.6, 43.6, 61.6, 160.5, 163.7. Anal. Calcd for $C_5H_8N_2O_2$: C, 46.87; H, 6.29; N, 21.86. Found: C, 46.81; H, 6.14; N, 22.16.

***trans*-(4*S*,5*R*)-5-Phenyl-2-oxazoline-4-(*N*-methoxy-*N*-methylcarboxamide) (7a).** Since the oxazoline is moisture sensitive, the solvents for chromatography (silica gel, 2.8 × 15 cm, hexane:EtOAC = 50:50−0:100) were dried over $CaCl_2$, and the supernatant was used directly without distillation. From 0.641 g (5.00 mmol) of **2** and 0.695 g (6.55 mmol) of **6a** was obtained 1.003 g (86%) of *trans*-(4*S*,5*R*)-**7a** as described in the text: mp 40−42 °C; $[\alpha]^{20}_D$ +287.2 (*c* 1.18, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 3.28 (s, 3 H), 3.72 (s, 3 H), 5.03 (d, J = 7.0 Hz, 1 H), 5.87 (d, J = 7.3 Hz, 1 H), 7.08 (d, J = 2.0 Hz, 1 H), 7.27−7.40 (m, 5 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 32.5, 61.7, 72.8, 81.8, 125.8, 128.5, 128.8, 139.3, 155.7, 170.0. Anal. Calcd for $C_{12}H_{14}N_2O_3$: C, 61.53; H, 6.02; N, 11.96. Found: C, 61.45; H, 6.07; N, 11.95.

***trans*-(4*S*,5*R*)-5-Methyl-2-oxazoline-4-(*N*-methoxy-*N*-methylcarboxamide) (7b).** A crude mixture of *trans*-(4*S*,5*R*)-**7b** and *cis*-**7b** (95:5) was obtained by the reaction of 0.641 g (5.00 mmol) of **2** and 0.6 mL (17 mmol) of **6b** in a quantitative yield and used for the preparation of **9b** without purification. An analytical sample was obtained by chromatography on silica gel: oil; $[\alpha]^{20}_D$ +304.6 (*c* 3.24, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.40 (d, J = 6.3 Hz, 3 H), 3.25 (s, 3 H), 3.82 (s, 3 H), 4.67 (br d, J = 5.4 Hz, 1 H), 4.94 (br quintet, J = 6 Hz, 1 H), 6.90 (d, J = 1.7 Hz, 1 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 20.2, 32.2, 61.4, 70.9, 77.0, 155.7, 170.3. Anal. Calcd for $C_7H_{12}N_2O_3$: C, 48.84; H, 7.02; N, 16.27. Found: C, 48.74; H, 6.87; N, 16.15.

***trans*-(4*S*,5*R*)-5-Isopropyl-2-oxazoline-4-(*N*-methoxy-*N*-methylcarboxamide) (7c).** From 0.641 g (5.00 mmol) of **2** and 0.485 g (6.73 mmol) of **6c** was obtained 0.901 g (90%) of *trans*-(4*S*,5*R*)-**7c**: oil; $[\alpha]^{20}_D$ +294.7 (*c* 1.35, $CHCl_3$): ^{1}H NMR ($CDCl_3$) δ 0.93 (d, J = 7.0 Hz, 3 H), 0.96 (d, J = 7.0 Hz, 3 H), 1.85 (octet, J = 6.7 Hz, 1 H), 3.26 (s, 3 H), 3.85 (s, 3 H), 4.6−4.9 (m, 2 H), 6.91 (d, J = 1.6 Hz, 1 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 17.2, 17.5, 31.7, 32.4, 61.7, 67.0, 85.6, 156.1, 170.5. Anal. Calcd for $C_9H_{16}N_2O_3$: C, 53.99; H, 8.05; N, 13.99. Found: C, 54.06; H, 8.22; N, 13.78.

***trans*-(4*S*,5*R*)-5-[(*E*)-1-Propenyl]-2-oxazoline-4-(*N*-methoxy-*N*-methylcarboxamide) (7d).** From 0.641 g (5.00 mmol) of **2** and 0.453 g (6.46 mmol) of **6d** was obtained 0.927 g (94%) of *trans*-(4*S*,5*R*)-**7d**: oil; $[\alpha]^{20}_D$ +300.9 (*c* 1.02, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.74 (dd, J = 6.0, 1.2 Hz, 3 H), 3.25 (s, 3 H), 3.81 (s, 3 H), 4.81 (d, J = 6.3 Hz, 1 H), 5.25 (dd, J = 8.0, 7.0 Hz, 1 H), 5.51 (ddq, J = 14.8, 8.0, 1.5 Hz, 1 H), 5.87 (dq, J = 14.8, 6.0 Hz, 1 H), 6.92 (d, J = 2.0 Hz, 1 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 17.5, 32.2, 61.6, 69.8, 81.2, 127.7, 131.1, 155.6, 170.0. Anal. Calcd for $C_9H_{14}N_2O_3$: C, 54.54; H, 7.12; N, 14.13. Found: C, 54.59; H, 7.21; N, 13.92.

***trans*-(4*S*,5*R*)-5-[(*E*)-3-(Benzyloxy)-1-propenyl]-2-oxazoline-4-(*N*-methoxy-*N*-methylcarboxamide) (7e).** From 0.624 g (4.87 mmol) of **2** and 0.949 g (5.39 mmol) of **6e** was obtained 1.196 g (82%) of *trans*-(4*S*,5*R*)-**7e**: oil; $[\alpha]^{20}_D$ +201.8 (*c* 1.01, $CHCl_3$): ^{1}H NMR ($CDCl_3$) δ 3.25 (s, 3 H), 3.81 (s, 3 H), 4.05 (d, J = 4.7 Hz, 2 H), 4.53 (s, 2 H), 4.85 (br d, J = 5.8 Hz, 1 H), 5.35 (br d, J = 6.5 Hz, 1 H), 5.81 (ddt, J = 15.5, 6.7, 1.2 Hz, 1 H), 5.94 (dt, J = 15.4, 4.8 Hz, 1 H), 6.92 (d, J = 2.1 Hz, 1 H), 7.25−7.37 (m, 5 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 32.3, 61.7, 69.2, 70.0, 72.4, 80.3, 127.5, 127.6, 128.3, 128.4, 130.9, 137.8, 155.6, 169.8; HRMS (FAB) calcd for $C_{16}H_{21}N_2O_4$ (M + H)$^+$ 305.1501, found 305.1512. Anal. Calcd for $C_{16}H_{20}N_2O_4$: C, 63.14; H, 6.62; N, 9.20. Found: C, 62.41; H, 6.68; N, 9.13.

(2*S*,3*R*)-*N*$^{\alpha}$-(*tert*-Butoxycarbonyl)-*N*-methoxy-*N*-methyl-2-amino-3-hydroxy-3-phenylpropionamide (9a). A solution of 1.723 g (7.37 mmol) of (4*S*,5*R*)-**7a** in 8 mL of concd HCl/MeOH (1:5, v:v) was heated at 50 °C for 3 h. After neutralization with 10% aqueous ammonia, the methanol and water were evaporated under reduced pressure. A small amount of water was further removed by the successive addition and evaporation of methanol followed by $CHCl_3$. The residue was dissolved in 25 mL of CH_2Cl_2 (a 40 μL aliquot was taken for the determination of the enantiomeric excess; a substantial amount of NH_4Cl remained insoluble) and cooled to 0 °C. $(Boc)_2O$ (3.33 g, 15.26 mmol) was added, and after the mixture was stirred for 10 min 4.2 mL (30 mmol) of Et_3N was added and the mixture was stirred at 0 °C for 30 min and at rt overnight. Then CH_2Cl_2 and 10% aqueous citric acid were added to the mixture and the aqueous phase was extracted

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twice with CH_2Cl_2. The combined organic phases were washed with saturated aqueous $NaHCO_3$, and the washing was extracted twice with CH_2Cl_2. The organic phases were combined, dried over Na_2SO_4, and evaporated. Chromatography of the residue on silica gel (3.5 × 17 cm, hexane:EtOAc = 2:1–1:1) gave 2.187 g (92%) of **9a**: mp 107–108 °C; $[\alpha]^{20}_D$ −25.0 (*c* 1.00, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.32 (s, 9 H), 3.20 (s, 3 H), 3.3–3.5 (br s, 1 H), 3.71 (s, 3 H), 4.95 (br d, *J* = ca 9 Hz, 1 H), 5.04 (d, *J* = 3.1 Hz, 1 H), 5.48 (br d, *J* = ca 9 Hz, 1 H), 7.2–7.45 (m, 5 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 28.1, 32.0, 55.1, 61.5, 73.5, 79.8, 126.1, 127.7, 128.2, 139.7, 155.5, 171.7. Anal. Calcd for $C_{16}H_{24}N_2O_5$: C, 59.24; H, 7.46; N, 8.64. Found: C, 59.05; H, 7.20; N, 8.69.

(2*S*,3*R*)-*N*^{α}-(*tert*-Butoxycarbonyl)-*N*-methoxy-*N*-methyl-2-amino-3-hydroxybutanamide (9b). Reaction of the crude mixture of *trans*-(4*S*,5*R*)-**7b** and *cis*-**7b** obtained by the reaction of 5.00 mmol of **2** and 10.7 mmol of **6b** gave a crude mixture of (2*S*,3*R*)-**9b** and (2*S**,3*S**)-**9b** in a quantitative yield, which was used for the preparation of **10b** without purification. An analytical sample was obtained from diastereomerically pure **7b**: oil; $[\alpha]^{20}_D$ −14.4 (*c* 1.03, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.23 (d, *J* = 6.3 Hz, 3 H), 1.45 (s, 9 H), 2.7–2.9 (br s, 1 H), 3.24 (s, 3 H), 3.78 (s, 3 H), 4.08 (br q, *J* = 6.3 Hz, 1 H), 4.68 (br d, *J* = ca 9 Hz, 1 H), 5.43 (br d, *J* = ca 9 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 19.4, 28.2, 32.0, 54.4, 61.5, 67.5, 79.4, 156.6, 172.1. Anal. Calcd for $C_{11}H_{22}N_2O_5$: C, 50.37; H, 8.45; N, 10.68. Found: C, 50.40; H, 8.17; N, 10.62.

(2*S*,3*R*)-*N*^{α}-(*tert*-Butoxycarbonyl)-*N*-methoxy-*N*-methyl-2-amino-3-hydroxy-4-methylpentanamide (9c). From 0.901 g (4.50 mmol) of (4*S*,5*R*)-**7c** was obtained 1.156 g (88%) of **9c**: oil; $[\alpha]^{20}_D$ +0.68 (*c* 1.03, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.98 (d, *J* = 6.6 Hz, 3 H), 1.03 (d, *J* = 6.6 Hz, 3 H), 1.44 (s, 9 H), 1.65–1.9 (m, 1 H), 2.76 (br s, 1 H), 3.24 (s, 3 H), 3.45 (dd, *J* = 8.8, 1.6 Hz, 1 H), 3.80 (s, 3 H), 4.91 (br d, *J* = ca 9 Hz, 1 H), 5.49 (br d, *J* = ca. 9 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 18.7, 18.9, 28.2, 30.6, 32.1, 51.3, 61.3, 76.4, 79.5, 155.9, 172.8. Anal. Calcd for $C_{13}H_{26}N_2O_5$: C, 53.78; H, 9.03; N, 9.65. Found: C, 53.72; H, 9.28; N, 9.68.

(2*S*,3*R*)-(*E*)-*N*^{α}-(*tert*-Butoxycarbonyl)-*N*-methoxy-*N*-methyl-2-amino-3-hydroxy-4-hexenamide (9d). From 0.927 g (4.68 mmol) of (4*S*,5*R*)-**7d** was obtained 1.135 g (84%) of **9d**: oil; $[\alpha]^{20}_D$ +1.84 (*c* 1.09, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.44 (s, 9 H), 1.71 (dd, *J* = 7.3, 1.4 Hz, 3 H), 2.82 (br s, 1 H), 3.23 (s, 3 H), 3.79 (s, 3 H), 4.36 (br d, *J* = ca. 5 Hz, 1 H), 4.76 (br d, *J* = ca. 9 Hz, 1 H), 5.42 (br d, *J* = ca. 9 Hz, 1 H), 5.52 (ddq, *J* = 15.3, 6.4, 1.4 Hz, 1 H), 5.80 (ddq, *J* = 15.3, 1.0, 6.4 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 17.6, 28.2, 32.0, 54.0, 61.4, 72.3, 79.7, 128.5, 129.1, 155.8, 171.5. Anal. Calcd for $C_{13}H_{24}N_2O_5$: C, 54.15; H, 8.39; N, 9.72. Found: C, 53.87; H, 8.61; N, 9.69.

(2*S*,3*R*)-(*E*)-*N*^{α}-(*tert*-Butoxycarbonyl)-*N*-methoxy-*N*-methyl-2-amino-6-(benzyloxy)-3-hydroxy-4-hexenamide (9e). From 1.112 g (3.66 mmol) of (4*S*,5*R*)-**7e** was obtained 1.221 g (85%) of **9e**: oil; $[\alpha]^{20}_D$ +8.46 (*c* 1.53, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.41 (s, 9 H), 2.95 (br s, 1 H), 3.23 (s, 3 H), 3.78 (s, 3 H), 4.04 (d, *J* = 5.2 Hz, 2 H), 4.43–4.54 (m, 1 H), 4.51 (s, 2 H), 4.80 (br s, *J* = 10.0 Hz, 1 H), 5.45 (br d, *J* = 10.0 Hz, 1 H), 5.80 (dd, *J* = 15.6, 5.2 Hz, 1 H), 5.93 (ddt, *J* = 15.6, 0.9, 4.8 Hz, 1 H), 7.22–7.35 (m, 5 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 28.2, 32.0, 53.6, 61.5, 69.8, 71.7, 72.0, 79.8, 127.5, 127.7, 128.3, 129.2, 130.7, 138.1, 155.8, 171.4; HRMS (FAB) calcd for $C_{20}H_{31}N_2O_6$ $(M + H)^+$ 395.2182, found 395.2197. Anal. Calcd for $C_{20}H_{30}N_2O_6$: C, 60.90; H, 7.67; N, 7.10. Found: C, 60.02; H, 7.68; N, 7.01.

(4*S*,5*R*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-(*N*-methoxy-*N*-methylcarbamoyl)-5-phenyloxazolidine (10a). A solution of 1.71 g (5.26 mmol) of **9a**, 1.14 g (10.9 mmol) of 2,2-dimethoxypropane, and 20.2 mg (0.106 mmol) of $TsOH·H_2O$ in 20 mL of benzene was heated under reflux for 2 h and then slowly distilled. After 2 h 0.42 g (4.07 mmol) of 2,2-dimethoxypropane was added and the distillation was continued until most of the starting material was converted to the acetonide. To the cooled mixture was added saturated aqueous $NaHCO_3$ and ether. The organic phase was separated, and the aqueous phase was extracted twice with ether. The combined organic phases were washed with brine, dried over $MgSO_4$, and evaporated. Chromatography of the residue on silica gel (2.3 × 20 cm, hexane:EtOAc = 2.5:1) gave 1.71 g (89%) of **10a**: mp 108–110 °C; $[\alpha]^{20}_D$ +38.0 (*c* 1.04, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.40 and 1.50 (2 s, 9 H), 1.71 and 1.76 (2 s, 3 H), 1.73 and 1.78 (2 s, 3 H), 2.94 and 3.16 (2 s, 3 H), 3.18 (s, 3 H), 4.76 and 4.85 (2 br d, *J* = 8.0 Hz, 1 H), 5.01 and 5.08 (2 d, *J* = 8.0 Hz, 1 H), 7.30–7.48 (m, 5 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 24.0 and 25.0 (2 s), 26.5 and 27.7 (2 s), 28.4 (s), 32.5 (s), 60.7 and 60.8 (2 s), 63.2 and 63.3 (2 s), 79.9 and 80.2 (2 s), 94.9 and 95.6 (2 s), 126.9 and 127.3 (2 s), 128.5 (s), 128.7 and 128.9 (2 s), 137.7 and 138.0 (2 s), 150.9 and 151.7 (2 s), 170.9 (s). Anal. Calcd for $C_{19}H_{28}N_2O_5$: C, 62.62; H, 7.74; N, 7.69. Found: C, 62.46; H, 7.63; N, 7.59.

(4*S*,5*R*)-3-(*tert*-Butoxycarbonyl)-4-(*N*-methoxy-*N*-methylcarbamoyl)-2,2,5-trimethyloxazolidine (10b). From a crude mixture of (2*S*,3*R*)-**9c** and (2*S**, 3*S**)-**9b** was obtained 1.076 g (71% based on **2**) of (4*S*,5*R*)-**10b** as described for the preparation of **10a**: oil; $[\alpha]^{20}_D$ −9.81 (*c* 1.40, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.40 and 1.41 (2 d, *J* = 6.0 Hz, 3 H), 1.41 and 1.48 (2 s, 9 H), 1.61 (s, 3 H), 1.63 and 1.67 (2 s, 3 H), 3.23 (s, 3 H), 3.74 and 3.80 (2 s, 3 H), 4.14 and 4.18 (2 quintet, *J* = 7.0 Hz, 1 H), 4.38 and 4.51 (2 d, *J* = 7.3, 6.5 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 19.3 and 19.4 (2 s), 23.9 and 25.0 (2 s), 26.8 and 28.1 (2 s), 28.3 (s), 32.3 (s), 60.9 and 61.0 (2 s), 63.08 and 63.14 (2 s), 74.1 and 74.4 (2 s), 80.0 and 80.2 (2 s), 94.3 and 94.8 (2 s), 151.1 and 151.8 (2 s), 170.2 and 170.9 (2 s). Anal. Calcd for $C_{14}H_{26}N_2O_5$: C, 55.61; H, 8.67; N, 9.26. Found: C, 55.43; H, 8.84; N, 9.29.

(4*S*,5*R*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-5-isopropyl-4-(*N*-methoxy-*N*-methylcarbamoyl)oxazolidine (10c). From 0.418 g (1.44 mmol) of **9c** was obtained 0.407 g (86%) of **10c** as described for the preparation of **10a**: mp 80–82 °C; $[\alpha]^{20}_D$ +13.1 (*c* 0.96, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.99 and 1.01 (2 d, *J* = 6.7 Hz, 6 H), 1.42 and 1.48 (2 s, 9 H), 1.59 and 1.61 (2 s, 6 H), 1.80–2.05 (m, 1 H), 1.64 and 1.65 (2 s, 3 H), 3.22 (s, 3 H), 3.73 and 3.82 (2 s, 3 H), 3.8–3.9 (2 d, 1 H), 4.52 and 4.66 (2 d, *J* = 6.5, 5.6 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 16.0 and 17.0 (2 s), 18.8 and 19.6 (2 s), 24.2 and 25.2 (2 s), 26.6 and 27.9 (2 s), 28.33 and 28.38 (2 s), 29.9 and 30.6 (2 s), 32.4 (s), 59.2 and 59.3 (2 s), 60.7 and 60.8 (2 s), 80.1 and 80.2 (2 s), 83.1 (s), 94.0 and 94.7 (2 s), 151.3 and 152.0 (2 s), 170.8 and 171.4 (2 s). Anal. Calcd for $C_{16}H_{30}N_2O_5$: C, 58.16; H, 9.15; N, 8.48. Found: C, 57.86; H, 9.43; N, 8.45.

(4*S*,5*R*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-(*N*-methoxy-*N*-methylcarbamoyl)-5-[(*E*)-1-propenyl]oxazolidine (10d). From 0.575 g (1.99 mmol) of **9d** was obtained 0.498 g (76%) of **10d** as described for the preparation of **10a**: mp 52–53 °C; $[\alpha]^{20}_D$ +5.68 (*c* 1.11, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.40 and 1.58 (2 s, 9 H), 1.62 and 1.66 (2 s, 3 H), 1.63 and 1.67 (2 s, 3 H), 1.74 (dd, *J* = 6.5, 1.5 Hz, 3 H), 3.22 (s, 3 H), 3.66 and 3.73 (2 s, 3 H), 4.43 and 4.47 (2 br t, *J* = 7.4, 7.6 Hz, 1 H), 4.58 and 4.66 (2 br d, *J* = 7.0 Hz, 1 H), 5.59 (ddq, *J* = 15.3, 7.9, 1.5 Hz, 1 H), 5.75–5.98 (m, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 17.7 (s), 24.2 and 25.2 (2 s), 26.8 and 28.1 (2 s), 28.4 (s), 32.5 (s), 61.25 and 61.38 (2 s), 61.36 and 61.51 (2 s), 78.9 and 79.4 (2 s), 80.2 and 80.5 (2 s), 94.5 and 95.1 (2 s), 128.4 (s), 131.5 and 131.9 (2 s), 151.1 and 151.8 (2 s), 170.5 and 171.2 (2 s). Anal. Calcd for $C_{16}H_{28}N_2O_5$: C, 58.52; H, 8.59; N, 8.53. Found: C, 58.34; H, 8.88; N, 8.49.

(4*S*,5*R*)-5-[(*E*)-3-(Benzyloxy)-1-propenyl]-3-(*tert*-butoxycarbonyl)-2,2-dimethyl-4-(*N*-methoxy-*N*-methylcarbamoyl)oxazolidine (10e). From 1.156 g (2.93 mmol) of **9e** was obtained 1.007 g (79%) of **10e** as described for the preparation of **10a**: oil; $[\alpha]^{20}_D$ +19.6 (*c* 0.93, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.40 and 1.48 (2 s, 9 H), 1.63 and 1.66 (2 s, 3 H), 1.65 and 1.67 (2 s, 3 H), 3.21 (s, 3 H), 3.65 and 3.73 (2 s, 3 H), 4.06 (d, *J* = 3.7 Hz, 2 H), 4.46–4.63 (m, 1 H), 4.52 (s, 2 H), 4.68–4.71 (2 br s, 1 H), 5.80–6.05 (m, 2 H), 7.21–7.42 (m, 5 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 24.2 and 25.3 (2 s), 26.8 and 28.1 (2 s), 28.3 (s), 32.4 (s), 61.1 and 61.2 (2 s), 61.6 and 61.7 (2 s), 69.3 (s), 72.0 and 72.1 (2 s), 78.0 and 78.5 (2 s), 80.2 and 80.5 (2 s), 94.7 and 95.3 (2 s), 127.46 (s), 127.53 (s), 128.3 (s), 129.2 and 129.5 (2 s), 131.1 and 131.4 (2 s), 138.0 (s), 151.0 and 151.7 (2 s), 170.1 and 170.7 (2 s); HRMS (FAB) calcd for $C_{23}H_{35}N_2O_6$ $(M + H)^+$ 435.2495, found 435.2482. Anal. Calcd for $C_{23}H_{34}N_2O_6$: C, 63.57; H, 7.89; N, 6.45. Found: C, 63.04; H, 7.97; N, 6.42.

(4S,5R)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-formyl-5-phenyloxazolidine (11a). The literature procedure for the preparation of optically active α-[(*tert*-butoxycarbonyl)amino] aldehydes was slightly modified as follows: To a suspension of 48.9 mg (1.29 mmol) of $LiAlH_4$ in 3 mL of ether was added 0.365 g (1.00 mmol) of **10a** with 7 mL of ether at 0 °C. The mixture was stirred at 0 °C for 20 min and hydrolyzed with a solution of 0.242 g (1.78 mmol) of $KHSO_4$ in 5 mL of water. After more ether was added, the aqueous phase was separated and extracted three times with ether. The combined organic phases were successively washed with 10% aqueous citric acid, saturated aqueous $NaHCO_3$, and brine and dried over $MgSO_4$. Evaporation of the solvent (0.3 mmHg) gave 0.304 g (99.6%) of crude **11a**: oil; ^1H NMR ($CDCl_3$) δ 1.42 and 1.52 (2 br s, 9 H), 1.70 and 1.77 (2 br s, 6 H), 4.09 and 4.23 (2 br d, J = ca. 7, 3 Hz, 1 H), 4.97 (d, J = 8.4 Hz, 1 H), 7.37 (s, 5 H), 9.53 and 9.60 (2 br d, J = ca. 2 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 25.1 and 25.8 (2 s), 26.0 and 27.1 (2 s), 28.0 (s), 71.1 (s), 75.9 (s), 81.4 (s), 94.4 and 95.4 (2 s), 126.3 (s), 128.6 (s), 128.7 (s), 136.4 (s), 150.7 and 152.2 (2 s), 196.7 (s). Anal. Calcd for $C_{17}H_{23}NO_4$: C, 66.86; H, 7.59; N, 4.59. Found: C, 66.58; H, 7.65; N, 4.59.

MPLC purification (silica gel, hexane:EtOAc = 2:1) gave **11a** with higher purity in 91% isolated yield. The ^1H NMR was almost identical with the crude **11a**: oil; $[\alpha]^{20}_D$ −29.4 (*c* 3.26, $CHCl_3$). Anal. Found: C, 66.77; H, 7.56; N, 4.58.

(4S,5R)-3-(*tert*-Butoxycarbonyl)-4-formyl-2,2,5-trimethyloxazolidine (11b). Prepared as described for the preparation of **11a**: yield of crude **11b** 97%; oil; ^1H NMR ($CDCl_3$) δ 1.36 (d, J = 6.0 Hz, 3 H), 1.42 and 1.46 (2 s, 9 H), 1.50 and 1.59 (2 s, 3 H), 1.59 and 1.65 (2 s, 3 H), 3.70 and 3.80 (2 dd, J = 8.6, 4.3 Hz and 8.6, 3.8 Hz, 1 H), 4.06 (dq, J = 8.6, 6.1 Hz, 1 H), 9.38 and 9.45 (2 d, J = 4.3 Hz and 3.8 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 17.7 (s), 25.0 and 25.8 (2 s), 26.2 and 27.3 (2 s), 28.1 (s), 69.9 and 70.1 (2 s), 71.0 (s), 81.3 (s), 94.1 and 95.0 (2 s), 150.9 and 152.5 (2 s), 197.4 (s). Anal. Calcd for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70; N, 5.76. Found: C, 58.73; H, 8.62; N, 6.30.

Isolated yield by bulb-to-bulb distillation, 91%: oil; $[\alpha]^{20}_D$ −62.1 (*c* 2.28, $CHCl_3$) (lit.[2e] $[\alpha]^{20}_D$ −65.8 (*c* 1.66, $CHCl_3$)). Anal. Found: C, 58.49; H, 8.87; N, 6.16.

(4S,5R)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-formyl-5-isopropyloxazolidine (11c). Prepared as described for the preparation of **11a**: yield of crude **11c** 99%; oil; ^1H NMR ($CDCl_3$) δ 0.97 (d, J = 6.8 Hz, 3 H), 0.99 (d, J = 6.7 Hz, 3 H), 1.42 and 1.49 (2 s, 9 H), 1.57 (s, 3 H), 1.57 and 1.63 (2 s), 1.90 (octet, J = 6.6 Hz, 1 H), 3.74 (dd, J = 7.7, 6.1 Hz, 1 H), 3.93 and 4.09 (2 br dd, J = ca. 7, ca. 4 Hz, 1 H), 9.55 and 9.49 (2 br dd, J = ca. 4 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 17.8 (s), 18.4 (s), 25.2 and 26.1 (2 s), 26.2 and 27.4 (2 s), 28.3 (s), 31.2 (s), 67.6 (s), 79.3 (s), 81.4 (s), 94.1 and 95.0 (2 s), 151.1 and 152.6 (2 s), 198.1 (s). Anal. Calcd for $C_{14}H_{25}NO_4$: C, 61.97; H, 9.29; N, 5.16. Found: C, 61.31; H, 9.38; N, 5.11.

Isolated yield by bulb-to-bulb distillation, 95%: oil; $[\alpha]^{20}_D$ −22.8 (*c* 2.15, $CHCl_3$). Anal. Found: C, 61.99; H, 9.51; N, 5.12.

(4S,5R)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-formyl-5-[(*E*)-1-propenyl]oxazolidine (11d). Prepared as described for the preparation of **11a**: yield of crude **11d** 98%; oil; ^1H NMR ($CDCl_3$) δ 1.41 and 1.51 (2 s, 9 H), 1.60 and 1.66 (2 s, 6 H), 1.74 (dd, J = 6.5, 1.5 Hz, 3 H), 3.88 and 3.99 (2 dd, J = 8.4, 4.2 Hz and 8.1, 3.5 Hz, 1 H), 4.34 (t, J = 8.2 Hz, 1 H), 5.51 (ddq, J = 15.3, 3.1, 1.5 Hz, 1 H), 5.85 (dq, J = 15.3, 6.5 Hz, 1 H), 9.38 and 9.46 (2 d, J = 4.1, 3.5 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 17.6 (s), 25.1 and 25.8 (2 s), 26.0 and 27.2 (2 s), 28.1 (s), 69.4 (s), 75.0 and 75.2 (2 s), 81.3 (s), 94.1 and 94.9 (2 s), 126.1 (s), 132.5 (s), 150.8 and 152.3 (2 s), 196.7 (s). Anal. Cacld for $C_{14}H_{23}NO_4$: C, 62.43; H, 8.61; N, 5.20. Found: C, 62.34; H, 8.90; N, 5.16.

Isolated yield by bulb-to-bulb distillation, 95%: oil; $[\alpha]^{20}_D$ −50.2 (*c* 2.14, $CHCl_3$). Anal. Found: C, 62.27; H, 8.46; N, 5.22.

(4S,5R)-5-[(*E*)-3-(Benzyloxy)-1-propenyl]-3-(*tert*-butoxycarbonyl)-2,2-dimethyl-4-formyloxazolidine (11e). Prepared as described for the preparation of **11a**: yield of crude **11e** 96%; oil; ^1H NMR ($CDCl_3$) δ 1.42 and 1.49 (2 s, 9 H), 1.60 and 1.66 (2 s, 6 H), 3.88−3.99 (m, 1 H), 4.05 (d, J = 5.1 Hz, 2 H), 4.44 (dd, J = 8.1, 6.5 Hz, 1 H), 4.52 (s, 2 H), 5.81 (ddt, J = 15.6, 6.4, 1.4 Hz, 1 H), 5.93 (dt, J = 15.6, 4.7 Hz, 1 H), 7.20−7.43 (m, 5 H), 9.38−9.48 and 9.48−9.53 (2 m, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 25.1 and 25.9 (2 s), 26.0 and 27.2 (2 s), 28.0 (s), 69.1 (s), 69.2 (s), 72.1 (s), 74.1 and 74.4 (2 s), 81.3 (s), 94.2 and 95.1 (2 s), 126.8 (s), 127.4 (s), 127.5 (s) 128.2 (s), 132.1 (s), 137.8 (s), 150.7 and 152.2 (2 s), 196.6 (s).

Isolated yield by PTLC (silica gel, hexane/EtOAc = 3:1), 80%: oil; $[\alpha]^{20}_D$ −9.64 (*c* 2.45, $CHCl_3$); HRMS (FAB) calcd for $C_{21}H_{30}NO_5$ $(M + H)^+$ 376.2124, found 376.2133. Anal. Calcd for $C_{21}H_{29}NO_5$: C, 67.18; H, 7.79; N, 3.73. Found: C, 66.09; H, 7.77; N, 3.75.

(4S,5R)-4-Acetyl-3-(*tert*-butoxycarbonyl)-2,2-dimethyl-5-phenyloxazolidine (12). To a solution of 0.367 g (1.007 mmol) of **10a** in 3.7 mL of THF was added a 0.88 mL (2.49 mmol) ether solution of methylmagnesium bromide (2.83 M) at 0 °C. The mixture was stirred at 0 °C for 45 min and then at rt for 40 h before an addition of 10% aqueous citric acid and ether. The aqueous phase was extracted twice with ether. The combined organic phases were washed successively with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and evaporated. PTLC purification (silica gel, hexane:EtOAc = 2:1) gave 0.319 g (99%) of **12**: mp 59−60 °C; $[\alpha]^{20}_D$ +7.0 (*c* 1.72, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.40 and 1.49 (2 br s, 9 H), 1.71 and 1.76 (2 br s, 6 H), 2.07 (br s, 3 H), 4.30 and 4.41 (2 br d, J = 8.9 Hz and 7.8 Hz, 1 H), 4.83 (br d, J = 8.1 Hz, 1 H), 7.39 (s, 5 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 24.3 and 25.0 (2 s), 26.0 and 27.2 (2 s), 27.8 and 28.5 (2 s), 28.0 (s), 71.8 and 72.3 (2 s), 78.9 and 79.2 (2 s), 80.6 (s), 94.5 and 95.4 (2 s), 126.4 (s), 128.5 (s), 128.8 (s), 137.0 (s), 150.5 and 151.8 (2 s), 204.2 (s). Anal. Calcd for $C_{18}H_{25}NO_4$: C, 67.69; H, 7.89; N, 4.39. Found: C, 67.39; H, 7.93; N, 4.30.

***N*$^{\alpha}$-Formyl-L-phenylalanine-*N*-methoxy-*N*-methylamide (13).** A mixture of 0.244 g (1.04 mmol) of (4*S*,5*R*)-**7a** and 0.107 g 5% Pd/C in 1.5 mL of ethanol was placed in a stainless micro autoclave and magnetically stirred at rt with H_2 at 140 atm for 45 h. After filtration through a pad of Celite, the solvent was evaporated to give 0.243 g (99%) of **13**, which was used without further purification: ^1H NMR ($CDCl_3$) δ 2.99 (dd, J = 13.6, 6.6 Hz, 1 H), 3.13 (dd, J = 13.6, 5.9 Hz, 1 H), 3.19 (s, 3 H), 3.69 (s, 3 H), 5.35 (br q, J = ca. 8 Hz, 1 H), 6.24 (br d, 1 H), 7.10−7.35 (m, 5 H), 8.15 (s, 1 H).

***N*$^{\alpha}$-(*tert*-Butoxycarbonyl)-L-phenylalanine-*N*-methoxy-*N*-methylamide (14).** A solution of 0.243 g (1.028 mmol) of **13** in 6 mL of concd HCl/MeOH (1:5, v/v) was stirred at 50 °C for 2 h. After neutralization with 10% aqueous ammonia, the water was evaporated under reduced pressure. A small amount of water was further removed by the successive addition and evaporation of methanol followed by $CHCl_3$. The residue was dissolved in 6 mL of CH_2Cl_2 (a 120 μL aliquot was converted to its N^{α}-(3,5-dinitrobenzoyl) derivative for the determination of the enantiomeric excess; 96% ee) and cooled to 0 °C. $(Boc)_2O$ (0.326 g, 1.49 mmol) was added, and after 10 min of stirring 0.42 mL (3.01 mmol) of Et_3N was added and stirred at 0 °C for 30 min and at rt for 20 h. To the mixture were added CH_2Cl_2 and 10% aqueous citric acid. The aqueous phase was separated and extracted twice with CH_2Cl_2. The combined organic phases were washed with saturated aqueous sodium bicarbonate, and the washing was extracted twice with CH_2Cl_2. The organic phases were combined, dried over sodium sulfate, and evaporated. PTLC purification gave 0.244 g (77%) of **14**: oil; ^1H NMR ($CDCl_3$) δ 1.39 (s, 9 H), 2.88 (dd, J = 13.5, 6.7 Hz, 1 H), 3.05 (dd, J = 13.5, 5.9 Hz, 1 H), 3.17 (s, 3 H), 3.66 (s, 3 H), 4.95 (br q, 1 H), 5.17 (br d, 1 H), 7.12−7.36 (m, 5 H).

Supplementary Material Available: Copies of ^1H and $^{13}C\{^1H\}$ NMR spectra for compounds **7e**, **9e**, **10e**, and **11e** (8 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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