

Asymmetric Synthesis of α -Amino Acids by Copper-Catalyzed Conjugate Addition of Grignard Reagents to Optically Active Carbamatoacrylates

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Abstract: Optically active ene carbamates were α -lithiated by lithium tetramethylpiperidide in the presence of trialkylstannyl chlorides to produce α -stannylated compounds. These underwent facile palladium-catalyzed couplings with acid chlorides to produce α -keto ene carbamates in good yield. Treatment of the α -stannyl ene carbamates with butyllithium followed by quenching with carbon dioxide and esterification gave optically active carbamatoacrylates. Copper-catalyzed addition of *tert*-butyl-, 1-naphthyl-, 2-propenyl-, *p*-methoxyphenyl-, (trimethylsilyl)methyl-, cyclohexyl-, 1-adamantyl-, and isopropyl Grignard reagents followed by quenching at -10 to 25 °C and removal of the protecting groups gave the corresponding α -amino acids in 70–90% yield and 73–97% ee. Quenching the reaction at low temperature resulted in little if any asymmetric induction.

Introduction

Some years ago, an efficient route to optically active ene carbamates via chromium carbene complexes was developed in these laboratories.¹ These proved to be useful substrates in the synthesis of a range of optically active compounds. Palladium(II)-assisted alkylation/carbonylation² was used in the synthesis of a relay to (+)-thienamycin, while palladium(II)-assisted alkylation/transmetalation (from tin)³ was used in the total synthesis of (+)-negamycin and (-)-5-*epi*-negamycin.⁴ These optically active ene carbamates also underwent highly diastereoselective photochemical [2 + 2] cycloadditions with chromium alkoxycarbene complexes to produce optically active cyclobutanones,⁵ a process used in the total synthesis of (+)-tetrahydrocerculenin, and optically active butenolides isolated from marine sponges.⁶

Another areas of interest in these laboratories are the synthesis of optically active α -amino acids⁷ and their incorporation into small peptides,⁸ again utilizing photochemical reactions of chromium aminocarbene complexes. There are now well over 700 known naturally occurring α -amino acids⁹ of which only a small fraction are proteinogenic. Many of these have a wide

range of biological activity by themselves or as critical components in larger bioactive systems. Added to this molecular set is a growing number of unnatural amino acids which have found wide spread use in the study of a variety of biological processes, including enzymatic mechanisms, probing of conformational properties of peptides, and enzymatic inhibition. As a result, a number of methods have been developed in the area of the asymmetric synthesis of amino acids,¹⁰ with the most studied being the homologation of optically active glycine equivalents in the α -position.¹¹ Elaboration of the β -carbon for the stereoselective synthesis of amino acids has received far less attention and has been limited, for the most part, to two major approaches: (1) catalytic asymmetric hydrogenation of dehydroalanine derivatives¹² and (2) β -modification of readily available amino acids,¹³ in particular serine. Modifications of chiral dehydroalanine derivatives by classical methods other than hydrogenation are relatively rare. These include cycloaddition¹⁴ and conjugate additions to α,β -unsaturated amino acid derivatives,¹⁵ with the latter case being much more limited. Herein we report the efficient α -carboxylation of ene carbamate **1** and its use in the synthesis of a range of unusual amino acids by the asymmetric conjugate addition of Grignard reagents.

Results and Discussion

The general approach developed is shown in eq 1 and required the efficient α -lithiation of ene carbamate **1**. Despite ample

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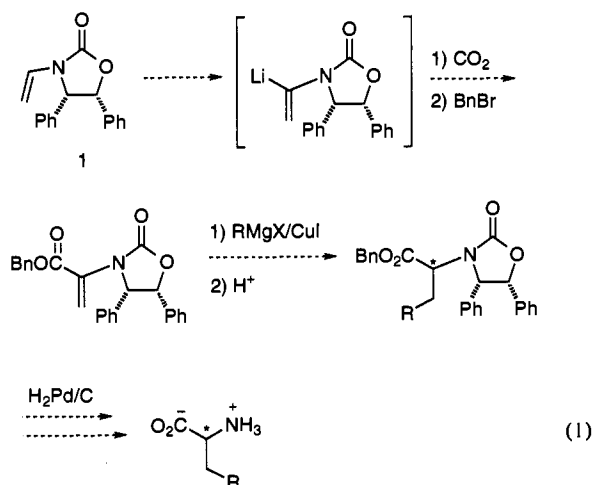
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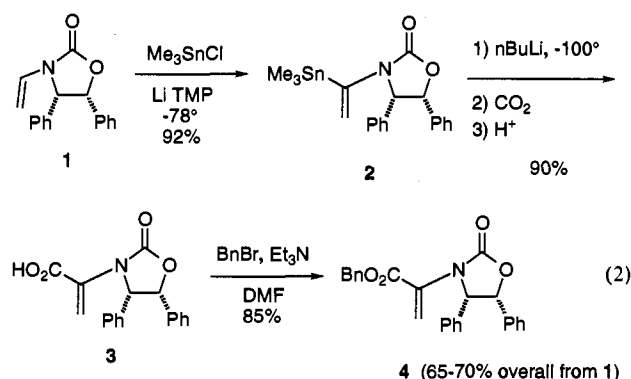
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literature precedent with closely related systems,¹⁶ this first step proved problematic. Use of *tert*-butyllithium, followed by quenching with a range of electrophiles, resulted in complex mixtures of products from which the expected products of α -lithiation could be isolated in only 25–50% yield. The use of *sec*-butyllithium or *n*-butyllithium under similar conditions gave competitive addition to the oxazolidinone carbonyl group. However, efficient lithiation/carboxylation was achieved in a two-step sequence proceeding through the stable and isolable vinyl stannane **2** (eq 2).¹⁷



Treatment of a mixture of **1** and trimethyltin chloride in THF at -78°C with freshly prepared lithium 2,2,6,6-tetramethylpiperide (Li(TMP)) gave stannane **2** in 92% yield. This metalation process was also effective with other ene carbamates, with tributylstannyl chloride, and with trimethylsilyl chloride (Table 1). Tin–lithium exchange of **2** with *n*-butyllithium occurred instantaneously at -100°C . Quenching with carbon dioxide at this temperature followed by warming to room temperature gave the desired acid **3** in excellent yield (other electrophiles such as methyl iodide, chloroformates, and di-*tert*-butoxy dicarbonate were much less effective, giving complex mixtures of products). Esterification with benzyl bromide gave the desired dehydroalanine **4** in 75–80% overall yield from **1**. When tin–lithium exchange was carried out at -78°C , the yields were 5 to 10% lower.

α -Stannylated ene carbamate **2** underwent facile palladium-catalyzed Stille coupling (eq 3)¹⁸ with acid chlorides under an atmosphere of carbon monoxide to produce enones **12** in fair

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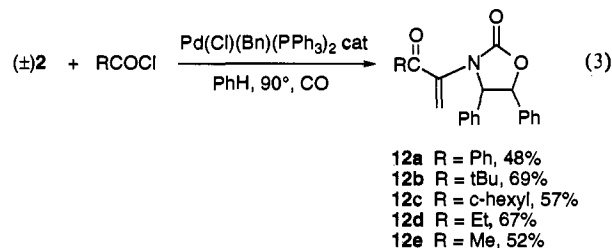
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Table 1. Synthesis of α -Metalated Ene Carbamates

Substrate	Electrophile	Product	Yield, %
1	Me ₃ SnCl	2	92
(\pm) 1	Me ₃ SnCl	2	94
5	Me ₃ SnCl	6 (M = Me ₃ Sn)	68
5	nBu ₃ SnCl	7 (M = Bu ₃ Sn)	71
(\pm) 1	Me ₃ SiCl	(\pm) 8	40
9	Me ₃ SnCl	10 (M = Me ₃ Sn)	80
9	nBu ₃ SnCl	11 (M = nBu ₃ Sn)	65

yield. These are potentially useful substrates for asymmetric



conjugate addition and cycloaddition processes, and their reactions will be reported elsewhere. When the reaction was carried out under argon rather than carbon monoxide, small amounts of decarbonylated products were obtained.



Conjugate additions to dehydroalanine **4** were next addressed.¹⁹ Although Me₂Cu(CN)Li₂ added effectively to **4** in a conjugate fashion, the diastereoselectivity of the overall process (addition/protonation of the enolate) was low ($\approx 2.5/1$). In contrast, the copper-catalyzed addition of Grignard reagents to **4** proceeded with excellent yield and with fair to excellent diastereoselectivity (eq 4, Table 2). Reductive removal (H₂, Pearlman's catalyst) of the benzyl ester and the oxazolidinone gave the corresponding free amino acid in excellent yield and high enantiomeric excess. As expected, the olefinic groups were reduced to the isopropyl (**13c** \rightarrow **14c**) and ethyl (**13d** \rightarrow **14d**) groups, respectively. Surprisingly,²⁰ the remote ring of the naphthyl group was reduced to the 5,6,7,8-tetrahydronaphthalene derivative, giving this unusual amino acid in excellent yield.

Several interesting features of this process were noted. Aryl and vinylic Grignard reagents added with virtually complete

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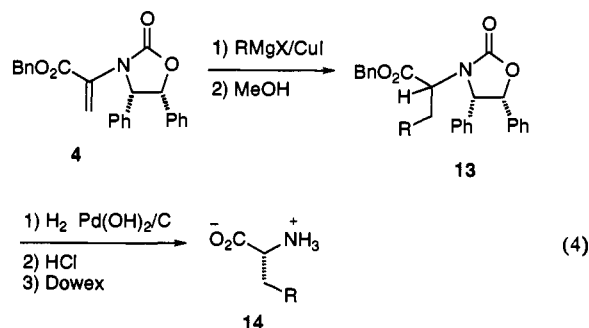
(20) Naphthalenes substituted in the 1-position are preferentially reduced at the substituted ring: Rylander, P. N. *Hydrogenation Methods*; Academic Press: New York, 1985; p 120.

Table 2. Synthesis of Amino Acids by Conjugate Alkylation of **4**

R	13	yield (%) ^a	ds ^b	R	14	yield (%) ^c	ee (%) ^d
<i>t</i> -butyl	13a	93	17.4:1 (16:1)	<i>t</i> -butyl	14a	90	89
	13b	95	>25:1 (>25:1)		14b	89	97
2-propenyl	13c	87	>25:1 (>25:1)	<i>i</i> -propyl	14c	90	88 ^e
vinyl	13d	74	>25:1 (>25:1)	ethyl	14d	91	92
<i>p</i> -MeOPh	13e	86	>25:1 (>25:1)	<i>p</i> -MeOPh	14e	93	97
TMSCH ₂	13f	82	12:1 (12:1)	TMSCH ₂	14f	97	88
<i>o</i> -hexyl	13g	75	>25:1 (9:1)	<i>o</i> -hexyl	14g	98	97
1-adamantyl	13h	75	6:1 (4:1)	1-adamantyl	14h	97	73
<i>i</i> -propyl	13i	89	10:1 (9:1)				

^a Reported yields are for isolated, purified mixtures of diastereoisomers.

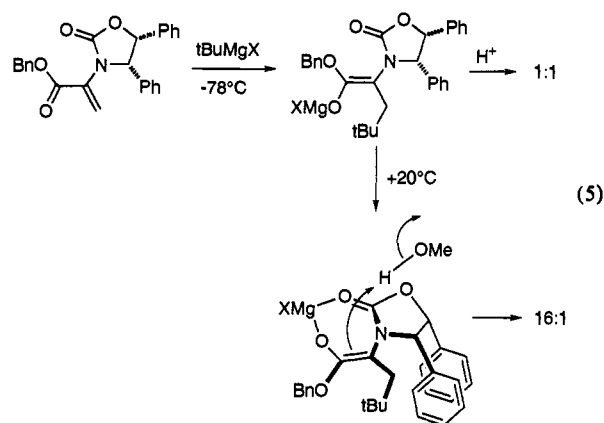
^b Estimated from ¹H NMR spectra of purified mixtures. Ratios in parentheses are those estimated from the crude reaction mixtures. ^c Yield of purified amino acid after ion-exchange chromatography. ^d Assessed by examination of the ¹⁹F NMR of the Mosher amides. ^e Stereochemical purity is lower than that of the material prior to reduction.



diastereoselectivity, and none of the minor diastereoisomer was detected by ¹H and ¹³C NMR spectroscopy of the crude reaction mixture. Aliphatic Grignard reagents added to **4** with varying degrees of stereoselectivity ranging from a low of 4:1 for adamantyl (**13h**) to a high of 16:1 for *tert*-butyl (**13a**). There was no apparent correlation between the steric bulk of the Grignard reagent and the stereoselectivity of the reaction. While the cyclohexyl adduct **12g** was dramatically enriched upon purification, little improvement in the diastereoisomeric ratio of the others was noted upon purification.

The effect of temperature on the degree of diastereoselectivity of protonation appears to be opposite of that typically associated with a process involving diastereomerically differentiated transition states. Higher temperatures of enolate hydrolysis gave *better* levels of stereoselectivity in the final products. For example, with *t*-BuMgCl, when methanol was added to the reaction mixture at $-78\text{ }^{\circ}\text{C}$, a 1:1 mixture of diastereoisomers was obtained. The ratio increased to approximately 16:1 when the hydrolysis was performed at room temperature. Running the addition reaction at $-78\text{ }^{\circ}\text{C}$ and warming to room temperature for 20 min followed by recooling to $-78\text{ }^{\circ}\text{C}$ and quenching with methanol at this temperature also gave a 16:1 ratio of diastereoisomers. It should be noted that the stereochemistry of the newly created stereogenic center is *not* set in the addition step, so arguments concerning steric hindrance to the approach of reagents are not an issue. Rather, the stereochemistry is determined in the protonation of the enolate resulting from conjugate addition and the specifics of this process are unknown. A possible rationale for these observations is shown in eq 5.²¹ Alkylation of the ene carbamate at $-78\text{ }^{\circ}\text{C}$ may produce the kinetically favored *E*-enolate which, lacking the rigidity imposed by chelation, undergoes stereorandom protonation. Warming this enolate to room temperature may promote isomerization to the *Z*-enolate which is stabilized by formation of the seven-membered magnesium chelate ring, with coordination of both the enolate oxygen and the oxazolidinone

(21) We thank a reviewer for suggesting this possibility.

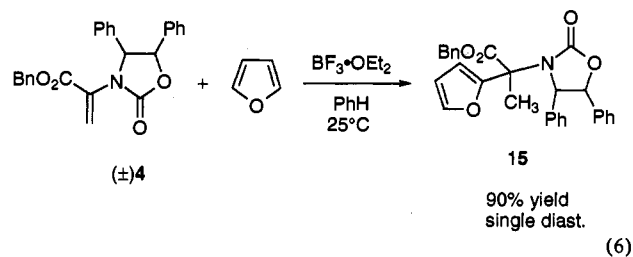


oxygen. This would lock the bulky *syn* phenyl groups in the "down" position. Protonation from the face opposite the phenyl groups leads to the stereochemistry observed.²² The validity of this model has not been established. In most of the relatively few reported cases of conjugate alkylations of dehydroamino acid derivatives,^{14,15} the disposition of the enone system with respect to the asymmetry inducing center(s) was firmly fixed by incorporation into a ring by *covalent* bonds. This is not the case with **4**.

In a very similar system²³ involving copper-catalyzed conjugate addition of phenyl Grignard reagents to acyclic acetamidoacrylate esters of optically active alcohols, a similar seven-membered chelate intermediate was proposed. However, in that case, the site of chirality was more remote from the new stereogenic center and rotation was not restricted, resulting in only modest diastereoselectivity (0–40% de).

The chemistry discussed herein represents the broadest reported application of this general methodology for the synthesis of optically active amino acids. The methodology most comparable and complementary in scope and efficiency is that of Vederas^{13a} utilizing the copper-assisted ring opening of serine-derived β -lactones by Grignard and organolithium reagents.

Dehydroalanine derivative **4** is also potentially useful for the synthesis of optically active α -methyl aryl glycines. By following the procedure reported for the Friedel Crafts alkylation of achiral α -acetamidoacrylates,²⁴ ene carbamate **4** was treated with boron trifluoride etherate and furan to give α -methyl-2-furylglycine **15** in 90% chemical yield as a single diastereoisomer (as determined from the ¹H NMR spectrum of the crude reaction mixture) (eq 6). The scope and limitations of this process will be reported in



due course.

Experimental Section

General Procedures. Melting points were taken on a Mel-Temp apparatus and are uncorrected. All ¹H NMR (300 MHz) and ¹³C NMR (75 MHz) spectra were obtained on a Bruker ACE-300 spectrometer

(22) The absolute configurations of the products in eq 4 were determined by comparison of the signs of rotation with those reported for known compounds (see the Experimental Section) and inferred from these for the remainder.

(23) Cativiela, C.; Diaz-de-Villegas, M. D.; Galvez, J. A. *Can. J. Chem.* **1992**, *70*, 2325.

(24) Cativieles, C.; Lopez, M. P.; Majoral, J. A. *Synlett* **1992**, 21.

unless noted otherwise. NMR spectra were recorded in CDCl_3 , D_2O , CD_3OD , or $\text{D}_2\text{O}/\text{CD}_3\text{OD}$, and chemical shifts are given in ppm relative to tetramethylsilane (0 ppm, ^1H), CDCl_3 (77.0 ppm, ^{13}C), D_2O (4.65 ppm, ^1H), or CD_3OD (49.0 ppm, ^{13}C). Infrared spectra were recorded on a Perkin-Elmer 1600 series FTIR. Optical rotations were obtained on a Rudolph Research automatic polarimeter Autopol III. Specific rotations ($[\alpha]_D$) are reported in degrees per decimeter, and the concentration (c) is given in grams per 100 mL in the specified solvent. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ. All reactions were performed under an atmosphere of argon unless otherwise noted. All glassware was flamed dried under vacuum and cooled under argon.

Silica gel (Silittech 32–63 μm) was purchased from ICN Biomedicals. Ion-exchange resin (Dowex 50X8-100) was purchased from Aldrich. THF (Malinkrodt) and Et_2O (Malinkrodt) were distilled from sodium/benzophenone under an atmosphere of nitrogen. DMF (Malinkrodt) was distilled from CaH_2 at aspirator pressure and stored over 4- \AA molecular sieves. Methanol (Malinkrodt) was stored over 3- \AA molecular sieves. Triethylamine (Aldrich) was distilled from CaH_2 and stored under argon. CH_2Cl_2 (technical grade) was distilled from CaH_2 and stored over 4- \AA molecular sieves. Pentanes (Malinkrodt) was stored over 4- \AA molecular sieves.

Trimethyltin chloride, tributyltin chloride, trimethylsilyl chloride, 1.6 M *n*-butyllithium in hexanes, 2,2,6,6-tetramethylpiperidine, 1.0 M *tert*-butylmagnesium chloride in THF, 1.0 M cyclohexylmagnesium chloride in Et_2O , 2.0 M isopropylmagnesium chloride in THF, 1.0 M vinylmagnesium bromide in Et_2O , 1.0 M ((trimethylsilyl)methyl)magnesium chloride in Et_2O , acetyl chloride, propionyl chloride, pivaloyl chloride, cyclohexylcarbonyl chloride, benzoyl chloride, 1-bromoadamantane, 1-bromonaphthalene, 2-bromopropene, *p*-bromoanisole, and Pearlman's catalyst ($\text{Pd}(\text{OH})_2$ on carbon 20% and 30% H_2O) were purchased from Aldrich and used without further purification. Benzyl bromide (Malinkrodt) and propylene oxide (Kodak) were used without further purification. Copper(I) iodide (Alpha) was recrystallized²⁵ and stored under argon. Mosher's acid was purchased from Aldrich and converted to the Mosher's acid chloride with oxalyl chloride and a catalytic amount of DMF in hexanes at reflux. $(\text{PPh}_3)_2\text{Pd}(\text{Bn})\text{Cl}$ was generated from $(\text{PPh}_3)_4\text{Pd}$ and benzyl chloride.²⁶

General Procedure for the Formation of 2 and 6–10. To a solution of the appropriate ene carbamate (1, 5, or 9) in THF under argon at -78°C was added 1.05–1.2 equiv of the trialkylmetal chloride, followed by addition of 1.25 equiv of freshly prepared lithium 2,2,6,6-tetramethylpiperide¹⁷ ($\text{Li}(\text{TMP})$) (approximately 0.8 M in hexanes/THF). The reaction was stirred at -78°C for 5–15 min then warmed to room temperature. To the reaction mixture was added an equal volume of Et_2O or $\text{Et}_2\text{O}/\text{CH}_2\text{Cl}_2$ (6:1). Subsequent extraction with H_2O (2 \times) and brine (1 \times) and drying (MgSO_4) gave the crude product after removal of the solvent. Column chromatography on silica gel gave the desired products as indicated in the individual experiment.

Preparation of Stannane 2 (Optically Active 4(R),5(S)-2). Optically active 4(R),5(S)-1 (1.33 g, 5.00 mmol), Me_3SnCl (1.20 g, 6.00 mmol) in THF (5 mL), and $\text{Li}(\text{TMP})$ (7.8 mL, 6.25 mmol, 0.8 M in hexanes/THF) were allowed to react in THF (25 mL). Workup and chromatography ($\text{SiO}_2/7:1$ hexanes:ethyl acetate) afforded 1.97 g (92%) of optically active 4(R),5(S)-2 as a white solid (mp = 65°C). ^1H NMR (CDCl_3 , TMS): δ 7.07 (m, 6H, ArH), 6.96 (m, 2H, ArH), 6.76 (m, 2H, ArH), 5.87 (d, $J = 8.0$ Hz, 1H, $\text{PhCHO}_{\text{oxa}}$), 5.34 (d, $J = 8.0$ Hz, 1H, $\text{PhCHN}_{\text{oxa}}$), 4.67 (s, 1H, =CHH), 4.51 (s, 1H, =CHH), 0.27 (s, 9H, $\text{Sn}(\text{CH}_3)_3$). ^{13}C NMR (CDCl_3): δ 157.0 (CO), 145.4, 133.7, 128.2, 128.1, 127.9, 127.8, 127.0, 126.4, 107.1, 80.4, 64.0, -6.3 . IR (NaCl, film): ν 3068, 3032, 2968, 2621, 1745, 1384, 1221 cm^{-1} . $[\alpha]_D = -87.6^\circ$ ($c = 1.5$, CHCl_3 , 25°C). This compound decomposed upon standing, and acceptable elemental analyses could not be obtained.

Preparation of Stannane (\pm)-2. Racemic 1 (2.65 g, 10.0 mmol), Me_3SnCl (2.19 g, 11.0 mmol) in THF (3 mL), and $\text{Li}(\text{TMP})$ (15.6 mL, 12.5 mmol, 0.8 M in hexanes/THF) were allowed to react in THF (40 mL). Subsequent workup and column chromatography ($\text{SiO}_2/7:1$ hexanes:ethyl acetate) gave 4.03 g (94%) of racemic 2 as a white solid (mp = 86 – 88°C). Spectroscopic data are identical to those reported for the optically active material.

Preparation of Stannane 6. Ene carbamate 5 (472 mg, 2.50 mmol), Me_3SnCl (548 mg, 2.75 mmol), and $\text{Li}(\text{TMP})$ (4.0 mL, 3.1 mmol, 0.8

M in hexanes/THF) were allowed to react in THF (10 mL). Subsequent workup and column chromatography ($\text{SiO}_2/7:1$ hexanes:ethyl acetate) gave 597 mg (68%) of 6 as a clear oil which solidified upon standing (mp = 63°C). ^1H NMR (CDCl_3 , TMS): δ 7.41–7.31 (m, 3H, ArH), 7.19 (m, 2H, ArH), 5.16 (dd, $J = 4.4, 9.0$ Hz, 1H, $\text{PhCHN}_{\text{oxa}}$), 4.69 (ap t, $J = 8.8$ Hz, 1H, CHHO), 4.67 (s, 1H, =CHH), 4.49 (s, 1H, =CHH), 4.10 (dd, $J = 4.4, 8.7$ Hz, CHHO), 0.23 (s, 9H, $\text{Sn}(\text{CH}_3)_3$). ^{13}C NMR (CDCl_3): δ 157.3 (CO), 145.4, 138.8, 129.2, 128.4, 125.6, 106.8, 70.4, 58.8, -6.4 . IR (NaCl, film): ν 3085, 3066, 3031, 2975, 2913, 1742 (CO), 1407, 1231, 1047 cm^{-1} . $[\alpha]_D = +36.0^\circ$ ($c = 1.2$, CHCl_3 , 25°C). Anal. Calcd for $\text{C}_{14}\text{H}_{19}\text{NO}_2\text{Sn}$: C, 47.77; H, 5.44; N, 3.98. Found: C, 48.00; H, 5.40; N, 3.86.

Preparation of Stannane 7. Ene carbamate 5 (472 mg, 2.50 mmol), *n*- Bu_3SnCl (746 μL , 2.75 mmol), and $\text{Li}(\text{TMP})$ (4.0 mL, 3.1 mmol, 0.8 M in hexanes/THF) were allowed to react in THF (10 mL). Subsequent workup and column chromatography ($\text{SiO}_2/7:1$ hexanes:ethyl acetate) gave 842 mg (71%) of 7 as a clear oil. ^1H NMR (CDCl_3 , TMS): δ 7.39–7.28 (m, 3H, ArH), 7.20 (m, 2H, ArH), 5.15 (dd, $J = 4.4, 9.0$ Hz, 1H, $\text{PhCHN}_{\text{oxa}}$), 4.71 (s, 1H, =CHH), 4.66 (ap t, $J = 8.8$ Hz, 1H, CHHO), 4.46 (s, 1H, =CHH), 4.07 (dd, $J = 4.4, 8.5$ Hz, CHHO), 1.58–1.49 (m, 6H, $-\text{CH}_2-$), 1.48–1.27 (m, 6H, $-\text{CH}_2-$), 1.03–0.95 (m, 6H, SnCH_2-), 0.92–0.87 (m, 9H, $-\text{CH}_3$). ^{13}C NMR (CDCl_3): δ 157.2 (CO), 145.1, 138.9, 129.1, 128.3, 125.6, 107.2, 70.3, 58.9, 29.0, 27.2, 13.6, 12.1. IR (NaCl, film): ν 1748 cm^{-1} . $[\alpha]_D = +41^\circ$ ($c = 1.2$, CHCl_3 , 25°C). Anal. Calcd for $\text{C}_{23}\text{H}_{37}\text{NO}_2\text{Sn}$: C, 57.76; H, 7.80; N, 2.93. Found: C, 58.00; H, 7.82; N, 2.83.

Preparation of Silane 8. Racemic 1 (130 mg, 0.49 mmol), Me_3SiCl (64 μL , 0.51 mmol), and $\text{Li}(\text{TMP})$ (0.73 mL, 0.51 mmol, 0.8 M in hexanes/THF) were allowed to react in THF (2 mL). Subsequent workup and column chromatography ($\text{SiO}_2/8:1$ hexanes:ethyl acetate) gave 66 mg (40%) of 8 as a clear oil. ^1H NMR (CDCl_3 , TMS): δ 7.07 (m, 6H, ArH), 6.94 (m, 2H, ArH), 6.78 (m, 2H, ArH), 5.89 (d, $J = 7.8$ Hz, 1H, PhCHO), 5.28 (d, $J = 7.9$ Hz, 1H, PhCHN), 4.75 (s, 1H, =CHH), 4.67 (s, 1H, =CHH), 0.29 (s, 9H, $\text{Si}(\text{CH}_3)_3$). ^{13}C NMR (CDCl_3): δ 155.7 (CO), 145.4, 134.0, 133.9, 128.2, 128.1, 127.9, 127.8, 126.9, 126.3, 110.0, 80.5, 64.7, 0.5. IR (NaCl, film): ν 1766 (CO), cm^{-1} . Anal. Calcd for $\text{C}_{20}\text{H}_{23}\text{NO}_2\text{Si}$: C, 71.18; H, 6.87; N, 4.15. Found: C, 71.08; H, 6.87; N, 3.94.

Preparation of Stannane 10. Ene carbamate 9 (537 mg, 2.50 mmol), Me_3SnCl (548 mg, 2.75 mmol), and $\text{Li}(\text{TMP})$ (4.0 mL, 3.1 mmol, 0.8 M in hexanes/THF) were reacted in THF (10 mL). Subsequent workup and column chromatography ($\text{SiO}_2/7:1$ hexanes:ethyl acetate) gave 750 mg (80%) of 10 as a clear oil which solidified upon standing (mp = 88°C). ^1H NMR (CDCl_3 , TMS): δ 7.38–7.25 (m, 3H, ArH), 7.16 (m, 2H, ArH), 5.47 (dd, $J = 3.9, 8.8$ Hz, 1H, $\text{PhC}(\text{N})\text{H}$), 4.64 (ap t, $J = 8.7$ Hz, 1H, $-\text{CHHO}$, *syn* to Ph), 4.07 (dd, $J = 3.9, 8.4$ Hz, 1H, $-\text{CHHO}$, *anti* to Ph), 1.11–1.00 (m, 3H, cyclopropyl H's), 0.48–0.42 (m, 1H, cyclopropyl H), 0.27 (s, 9H, $\text{Sn}(\text{CH}_3)_3$). ^{13}C NMR (CDCl_3): δ 157.5, 140.8, 129.0, 128.0, 125.2, 115.5, 70.3, 59.3, 5.4, 3.6, -5.6 . IR (NaCl, film): ν 1738 (CO) cm^{-1} . $[\alpha]_D = +20^\circ$ ($c = 1.7$, CHCl_3 , 25°C). Anal. Calcd for $\text{C}_{16}\text{H}_{21}\text{NO}_2\text{Sn}$: C, 50.84; H, 5.60; N, 3.71. Found: C, 50.63; H, 5.68; N, 3.58.

Preparation of Stannane 11. Ene carbamate 9 (537 mg, 2.50 mmol), *n*- Bu_3SnCl (746 μL , 2.75 mmol), and $\text{Li}(\text{TMP})$ (4.0 mL, 3.1 mmol, 0.8 M in hexanes/THF) were allowed to react in THF (10 mL). Subsequent workup and column chromatography ($\text{SiO}_2/7:1$ hexanes:ethyl acetate) gave 821 mg (65%) of 11 as a clear oil. ^1H NMR (CDCl_3 , TMS): δ 7.35–7.26 (m, 3H, ArH), 7.17 (m, 2H, ArH), 5.46 (dd, $J = 4.3, 8.8$ Hz, 1H, $\text{PhC}(\text{N})\text{H}$), 4.63 (ap t, $J = 8.7$ Hz, 1H, $-\text{CHHO}$, *syn* to Ph), 4.06 (dd, $J = 4.3, 8.4$ Hz, 1H, $-\text{CHHO}$, *anti* to Ph), 1.57–0.86 (m, 30H, $\text{Sn}(\text{n-Bu})_3$ and cyclopropyl H's), 0.46 (m, 1H, cyclopropyl H). ^{13}C NMR (CDCl_3): δ 157.4, 140.9, 128.9, 128.0, 126.5, 125.4, 115.7, 76.2, 59.6, 29.1, 27.4, 13.7, 12.6, 6.0, 3.7. IR (NaCl, film): ν 3031, 2955, 2920, 1745 (CO), 1450, 1266, 1060, 1046 cm^{-1} . $[\alpha]_D = +5^\circ$ ($c = 1.5$, CHCl_3 , 25°C). This compound decomposed on standing, and acceptable elemental analyses could not be obtained.

General Procedure for the Pd(0)-Catalyzed Cross Coupling of Acid Halides and Racemic 2, Formation of 12a–e. To a solution of racemic 2 in benzene was added 0.9–1.1 equiv of the requisite acid chloride followed by addition of $(\text{Ph}_3\text{P})_2\text{Pd}(\text{Bn})\text{Cl}$. The reaction was flushed with CO (2 \times), then pressurized to 30–40 psi of CO and allowed to stir for 3–24 h at 90–110 $^\circ\text{C}$. When a palladium mirror or palladium black formed, indicating reaction completion, the reaction was cooled to room temperature and vented. The mixture was then filtered through a plug of silica gel eluting with 1:1 diethyl ether:methylene chloride. Removal of the solvent followed by column chromatography (SiO_2) using hexanes:

(25) Dieter, K. R.; Silks, L. A.; Fishpugh, J. R.; Kastner, M. E. *J. Am. Chem. Soc.* 1985, 107, 4679.

(26) Fitton, P.; M^cKeon, J. E.; Beau, B. C. *J. Chem. Soc., Chem. Commun.* 1969, 370.

ethyl acetate as the eluent gave products **12a–e** as indicated in the individual experiments.

12a. As described in the general procedure, racemic **2** (450 mg, 1.05 mmol), benzoyl chloride (116 μ L, 1.00 mmol), and Pd(PPh₃)₂(Bn)Cl (39 mg, 5 mol %) in benzene (2 mL) were allowed to react at 110 °C for 24 h under 35 psi of carbon monoxide. Chromatography (SiO₂/4:1 hexanes:ethyl acetate) afforded 190 mg (51%) of **11a** as a white solid (mp = 160.5–161 °C). ¹H NMR (CDCl₃, TMS): δ 7.66 (m, 2H, ArH), 7.51 (m, 1H, ArH), 7.39–7.34 (m, 2H, ArH), 7.12–7.06 (m, 6H, ArH), 7.03 (m, 2H, ArH), 6.92 (m, 2H, ArH), 6.03 (d, J = 8.1 Hz, 1H, PhC(O)H), 5.71 (d, J = 1.6 Hz, 1H, =CHH), 5.58 (d, J = 8.2 Hz, 1H, PhC(N)H), 5.25 (d, J = 1.7 Hz, 1H, =CHH). ¹³C NMR (CDCl₃): δ 191.3, 155.5, 140.3, 136.2, 134.0, 133.8, 133.1, 129.8, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 126.1, 114.3, 80.1, 64.8. IR (NaCl, film): ν 1760 (CO), 1670 (CO) cm⁻¹. Anal. Calcd for C₂₄H₁₉NO₃: C, 78.03; H, 5.18; N, 3.79. Found: C, 77.87; H, 5.41; N, 3.73.

12b. As described in the general procedure racemic **2** (159 mg, 0.37 mmol), pivaloyl chloride (46 μ L, 0.37 mmol), and Pd(PPh₃)₂(Bn)Cl (11 mg, 0.015 mmol) in benzene (1 mL) were heated at 90 °C for 5.5 h under 30 psi of carbon monoxide. Chromatography (SiO₂/4:1:1 hexanes:ethyl acetate:dichloromethane) afforded 89 mg (69%) of **12b** as an oil. ¹H NMR (CDCl₃, TMS): δ 7.09 (m, 6H, ArH), 6.97–6.91 (m, 4H, ArH), 5.97 (d, J = 8.2 Hz, 1H, PhC(O)H), 5.33 (d, J = 8.2 Hz, 1H, PhC(N)H), 4.73 (d, J = 2.3 Hz, 1H, =CHH), 4.62 (d, J = 2.3 Hz, 1H, =CHH), 1.28 (s, 9H, C(CH₃)₃). ¹³C NMR (CDCl₃): δ 206.7, 154.8, 140.2, 133.7, 133.2, 128.5, 128.3, 128.2, 127.9, 127.3, 126.2, 101.7, 80.8, 64.5, 44.3, 27.7. IR (NaCl, film): ν 1755, 1692 cm⁻¹. Anal. Calcd for C₂₂H₂₃NO₃: C, 75.62; H, 6.63; N, 4.01. Found: C, 75.46; H, 6.51; N, 4.06.

12c. As described in the general procedure, racemic **2** (214 mg, 0.50 mmol), cyclohexylcarbonyl chloride (67 μ L, 0.50 mmol), and Pd(PPh₃)₂(Bn)Cl (7.8 mg, 0.01 mmol) in benzene (0.5 mL) were heated at 100 °C for 3.5 h under 30 psi of carbon monoxide. Chromatography (SiO₂/4:1 hexanes:ethyl acetate) afforded 105 mg (57%) of **12c** as an oil. ¹H NMR (CDCl₃, TMS): δ 7.12–6.96 (m, 8H, ArH), 6.82 (m, 2H, ArH), 5.98 (d, J = 8.4 Hz, 1H, PhC(O)H), 5.76 (d, J = 1.6 Hz, 1H, =CHH), 5.72 (d, J = 1.6 Hz, 1H, =CHH), 5.57 (d, J = 8.2 Hz, 1H, PhC(N)H), 2.78 (ap t, J = 11.3, 3.3 Hz, 1H, (CH₂)₂CHCO), 1.82–0.87 (m, 10H, ring CH₂'s). ¹³C NMR (CDCl₃): δ 200.9, 156.1, 140.6, 134.3, 133.9, 128.3, 128.2, 128.0, 127.9, 127.8, 126.0, 116.3, 79.9, 65.0, 46.0, 29.5, 28.5, 25.8, 25.7, 25.4. IR (NaCl, film): ν 1760, 1698 cm⁻¹. Anal. Calcd for C₂₄H₂₅NO₃: C, 76.77; H, 6.71; N, 3.73. Found: C, 76.54; H, 6.66; N, 3.67.

12d. As described in the general procedure, racemic **2** (162 mg, 0.38 mmol), propionyl chloride (37 μ L, 0.40 mmol), and Pd(PPh₃)₂(Bn)Cl (12 mg, 0.015 mmol) in benzene (1 mL) were heated at 90 °C for 21 h under 30 psi of carbon monoxide. Chromatography (SiO₂/4:1 hexanes:ethyl acetate) afforded 82 mg (67%) of **12d** as an oil. ¹H NMR (CDCl₃, TMS): δ 7.11–7.05 (m, 6H, ArH), 6.86–6.82 (m, 4H, ArH), 6.00 (d, J = 8.3 Hz, 1H, PhC(O)H), 5.81 (d, J = 1.7 Hz, 1H, =CHH), 5.73 (d, J = 1.7 Hz, 1H, =CHH), 5.60 (d, J = 8.3 Hz, 1H, PhC(N)H), 2.75–2.50 (m, 2H, OCC(=O)Me), 1.04 (t, J = 7.3 Hz, 3H, CH₂CH₃). ¹³C NMR (CDCl₃): δ 198.1, 156.2, 141.1, 134.3, 133.9, 128.3, 128.2, 128.1, 127.9, 127.8, 126.0, 117.5, 80.1, 65.2, 31.8, 8.0. IR (NaCl, film): ν 1760, 1697 cm⁻¹. Anal. Calcd for C₂₆H₁₉NO₃: C, 74.75; H, 5.96; N, 4.36. Found: C, 74.65; H, 6.08; N, 4.30.

12e. As described in the general procedure, racemic **2** (219 mg, 0.51 mmol), acetyl chloride (40 μ L, 0.56 mmol), and Pd(PPh₃)₂(Bn)Cl (16 mg, 0.02 mmol) in benzene (1 mL) were heated at 90 °C for 9 h under 30 psi of carbon monoxide. Chromatography (SiO₂/4:1 hexanes:ethyl acetate) afforded 82 mg (52%) of **12e** as an oil. ¹H NMR (CDCl₃, TMS): δ 7.11–7.06 (m, 6H, ArH), 6.99 (m, 2H, ArH), 6.84 (m, 2H, ArH), 6.01 (d, J = 8.3 Hz, 1H, PhC(O)H), 5.91 (d, J = 1.7 Hz, 1H, =CHH), 5.84 (d, J = 1.7 Hz, 1H, =CHH), 5.62 (d, J = 8.3 Hz, 1H, PhC(N)H), 2.29 (s, 3H, OCC(=O)Me). ¹³C NMR (75 MHz, CDCl₃): δ 194.8, 141.2, 134.2, 133.9, 128.3, 128.2, 128.0, 127.9, 127.7, 126.0, 119.7, 80.1, 65.3, 26.3. IR (NaCl, film): ν 1758, 1697 cm⁻¹. Anal. Calcd for C₁₉H₁₇NO₃: C, 74.25; H, 5.57; N, 4.56. Found: C, 74.36; H, 5.70; N, 4.42.

Synthesis of 4(R),5(S)-Carbamatoacrylate 4. To a stirred solution of 4(R),5(S)-**2** (808 mg, 1.88 mmol) in 12 mL of 4:1:1 THF:Et₂O:pentane at –100 °C under argon was added *n*-BuLi (1.47 mL, 2.35 mmol, 1.6 M in hexanes). After the mixture was stirred for 30 min, an excess of freshly crushed CO₂(s) was added under a positive flow of argon. The cooling bath (ether/liquid N₂) was removed, and the reaction was allowed to warm to room temperature. Wet diethyl ether (30 mL) was added, and the reaction was extracted with a 0.5 N NaOH solution (2 \times 20 mL). The aqueous layers were combined and acidified with 2 N HCl until the

pH was below 4. The acidic solution was extracted with ethyl acetate (3 \times 30 mL). The ethyl acetate fractions were combined, dried over anhydrous Na₂SO₄, filtered, and concentrated by rotary evaporation to give acid **3**, which was used without any further purification. The crude acid **3** was dissolved in DMF (10 mL), followed by addition of benzyl bromide (0.455 mL, 3.76 mmol) and triethyl amine (0.523 mL, 3.76 mmol), and allowed to stir for 19 h. Water (25 mL) was added, and the mixture was extracted with ethyl acetate (3 \times 25 mL). The combined organic extracts were washed with H₂O (3 \times 50 mL) and brine (75 mL) and dried (Na₂SO₄). Column chromatography (SiO₂/3:1 hexanes:ethyl acetate) afforded 0.603 g (80%) of 4(R),5(S)-**4** as a clear oil which solidified upon standing (mp = 72 °C). ¹H NMR (CDCl₃, TMS): δ 7.36 (m, 5H, ArH), 7.07 (m, 6H, ArH), 6.95 (m, 2H, ArH), 6.83–6.80 (m, 2H, ArH), 6.09 (d, J = 0.9 Hz, 1H, =CHH), 5.95 (d, J = 8.4 Hz, 1H, PhC(O)H_{oxa}), 5.65 (d, J = 0.9 Hz, 1H, =CHH), 5.62 (d, J = 8.4 Hz, 1H, PhC(N)H_{oxa}), 5.25 (d, J = 12.3 Hz, 1H, PhCH₂O), 5.19 (d, J = 12.3 Hz, 1H, PhCHHO). ¹³C NMR (CDCl₃): δ 162.9 (CO_{oxa}), 156.0 (CO_{oxa}), 135.1, 134.1, 133.6, 133.5, 128.6, 128.4, 128.3, 128.2, 128.18, 128.0, 127.9, 127.7, 126.0, 120.3, 80.0, 67.5, 65.8. IR (NaCl, film): ν 1766 (CO), 1731 (CO) cm⁻¹. [α]_D = +44° (*c* = 1.0, CHCl₃, 26 °C). Anal. Calcd for C₂₅H₂₁NO₄: C, 75.17; H, 5.30; N, 3.51. Found: C, 75.31; H, 5.49; N, 3.55.

By following the same procedure, racemic **2** (3.00 g, 7.01 mmol) gave 2.13 g (76%) of racemic **4** as a white solid (mp = 98–101 °C). Spectroscopic data were identical to those of the optically active 4(R),5(S)-**4**.

General Procedure for CuI-mediated Conjugate Addition of Grignard Reagents to 4. To a solution/suspension of 4/copper(I) iodide in THF under argon at –78 °C was added the Grignard reagent. The reaction was allowed to stir at –78 °C for 1.7–2 h and then adjusted to the appropriate temperature (–10 °C to room temperature) and allowed to stir for an additional 30 min. Methanol was then rapidly added via syringe, and the reaction was warmed to room temperature. The entire reaction mixture was passed through a plug of silica gel with the aid of 1:1 hexanes:ethyl acetate. Removal of the solvent by rotary evaporation gave the crude material from which the diastereoselectivity was estimated. Purification by flash chromatography or recrystallization gave the desired products as indicated in the individual experiments.

13a. According to the general procedure, 4(R),5(S)-**4** (100 mg, 0.25 mmol), CuI (24 mg, 0.13 mmol), and *t*-BuMgCl (0.50 mL, 0.50 mmol, 1.0 M in THF) were allowed to react at –78 °C for 2 h then at room temperature for 30 min. Methanol (100 μ L) was added, and the reaction was passed through a plug of silica gel eluting with 1:1 hexanes:ethyl acetate. Removal of the solvent gave the crude product as a mixture of diastereomers (approximately 16:1 ds by ¹H NMR). Chromatography (SiO₂/7:1 hexanes:ethyl acetate) gave 106 mg (93%) of **13a** as a clear oil and a 17.4:1 mixture of diastereomers (¹H NMR). ¹H NMR (CDCl₃, TMS): δ 7.33 (m, 3H, ArH), 7.23 (m, 2H, ArH), 7.08–6.94 (m, 8H, ArH), 6.85 (dd, J = 1.4, 7.5 Hz, 1H, ArH), 5.79 (d, J = 8.1 Hz, 1H, PhC(O)H_{oxa}), 5.11 (d, J = 8.1 Hz, PhC(N)H_{oxa}), 4.73 (d, J = 12.6 Hz, 1H, PhCHHO), 4.55 (d, J = 12.3 Hz, 1H, PhCH₂O), 4.40 (dd, J = 6.0, 6.9 Hz, 1H, α -H), 2.18 (dd, J = 6.6, 14.4 Hz, β -CHH), 1.88 (dd, J = 5.7, 14.4 Hz, β -CHH), 0.90 (s, 9H, C(CH₃)₃). ¹³C NMR (CDCl₃): δ 170.0 (CO_{oxa}), 157.7 (CO_{oxa}), 135.0, 134.4, 134.0, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 125.9, 80.0, 66.8, 64.2, 53.7, 42.6, 30.2, 29.4. IR (NaCl, film): ν 1759 (CO), 1746 (CO) cm⁻¹. Anal. Calcd for C₂₉H₃₁NO₄: C, 76.12; H, 6.83; N, 3.06. Found: C, 76.04; H, 6.92; N, 3.05.

13b. According to the general procedure 4(R),5(S)-**4** (100 mg, 0.25 mmol), CuI (24 mg, 0.13 mmol), and freshly prepared 1-naphthylmagnesium bromide (1.0 mL, 0.50 mmol, 0.5 M in THF) were allowed to react in THF (4 mL) at –78 °C for 2 h then at –10 °C for 0.5 h. Methanol (100 μ L) was added at –10 °C, then reaction was warmed to room temperature and passed through a plug of silica gel eluting with 1:1 hexanes:ethyl acetate. Removal of the solvent gave the crude product as a single diastereomer (by ¹H NMR). Chromatography (silica gel/5:1 hexanes:ethyl acetate) gave 126 mg (95%) of **13b** as a white solid (mp = 179 °C) (single diastereoisomer by ¹H NMR). ¹H NMR (CDCl₃, TMS): δ 7.84 (d, J = 8.4 Hz, 2H, ArH), 7.78 (d, J = 8.1 Hz, 1H, ArH), 7.58 (d, J = 8.1 Hz, 1H, ArH), 7.47–7.25 (m, 9H, ArH), 6.97 (d, J = 5.1 Hz, 1H, ArH), 6.90 (ap t, J = 9.2 Hz, 2H, ArH), 6.71 (ap t, J = 7.5 Hz, 1H, ArH), 6.60 (d, J = 7.2 Hz, 2H, ArH), 6.34 (bs, 2H, ArH), 5.60 (bs, 1H, ArH), 5.55 (d, J = 8.4 Hz, 1H, PhC(O)H_{oxa}), 5.30 (d, J = 12.3 Hz, 1H, PhCHHO), 5.23 (d, J = 8.7 Hz, PhC(N)H_{oxa}), 5.19 (d, J = 12.3 Hz, 1H, PhCH₂O), 4.36 (dd, J = 12.3, 14.7 Hz, 1H, α -H), 3.97–3.91 (m, 2H, β -CH₂). ¹³C NMR (CDCl₃): δ 169.8 (CO_{oxa}), 159.0 (CO_{oxa}), 135.2, 134.6, 133.8, 133.4, 132.2, 131.8, 128.8, 128.7, 128.5,

128.2, 127.8, 127.7, 127.5, 127.4, 126.3, 126.1, 125.5, 125.47, 123.1, 79.5, 67.6, 67.1, 57.7, 31.6. IR (NaCl, film): ν 1744 (both CO's) cm^{-1} . $[\alpha]_{\text{D}}^{25} = +251.0^\circ$ ($c = 0.43$, CHCl_3 , 25°C). Anal. Calcd for $\text{C}_{35}\text{H}_{29}\text{NO}_4$: C, 79.68; H, 5.54; N, 2.65. Found: C, 79.74; H, 5.60; N, 2.62.

13c. According to the general procedure 4(R),5(S)-4 (100 mg, 0.25 mmol), CuI (24 mg, 0.13 mmol), and freshly prepared 2-propenylmagnesium bromide (0.38 mL, 0.38 mmol, 1.0 M in THF) were allowed to react in THF (4 mL) at -78°C for 105 min then at -10°C for 30 min. Methanol (100 μL) was added at -10°C , and the reaction was warmed to room temperature and then passed through a plug of silica gel eluting with 1:1 hexanes:ethyl acetate. Removal of the solvent gave the crude product as a single diastereomer (by ^1H NMR). Chromatography (silica gel/7:1 hexanes:ethyl acetate) gave 96 mg (87%) of **13c** as a white solid, mp = 138°C (single diastereoisomer by ^1H NMR). ^1H NMR (CDCl_3 , TMS): δ 7.39–7.25 (m, 5H, ArH), 7.10–6.98 (m, 6H, ArH), 6.92 (m, 2H, ArH), 6.85 (d, $J = 6.9$ Hz, 2H, ArH), 5.75 (d, $J = 8.7$ Hz, 1H, PhC(O) H_{oxa}), 5.18 (d, $J = 8.4$ Hz, 1H, PhC(N) H_{oxa}), 4.97–4.93 (m, 3H, C=CH₂ and PhCH₂O), 4.80 (d, $J = 12.6$ Hz, 1H, PhCH₂O), 4.28 (dd, $J = 5.1, 10.5$ Hz, 1H, α -H), 3.03 (dd, $J = 10.5, 14.4$ Hz, 1H, β -CHH), 2.64 (dd, $J = 5.1, 14.4$ Hz, 1H, β -CHH), 1.63 (s, 3H, CH₃). ^{13}C NMR (CDCl_3): δ 169.6 (CO_{ester}), 158.1 (CO_{oxa}), 140.8, 135.0, 134.6, 133.6, 128.5, 128.4, 128.35, 128.3, 128.0, 127.9, 127.8, 127.7, 126.0, 114.5, 79.9, 67.1, 64.7, 54.6, 36.9, 21.9. IR (NaCl, film): ν 1741 (both CO's) cm^{-1} . $[\alpha]_{\text{D}}^{25} = +111^\circ$ ($c = 1.0$, CHCl_3 , 25°C). Anal. Calcd for $\text{C}_{28}\text{H}_{27}\text{NO}_4$: C, 76.17; H, 6.16; N, 3.17. Found: C, 76.12; H, 6.28; N, 3.11.

13d. According to the general procedure 4(R),5(S)-4 (100 mg, 0.25 mmol), CuI (24 mg, 0.13 mmol), and vinylmagnesium bromide (0.32 mL, 0.31 mmol, 1.0 M in THF) were allowed to react in THF (4 mL) at -78°C for 120 min then at -10°C for 30 min. Methanol (100 μL) was added at -10°C , and the reaction was then warmed to room temperature and passed through a plug of silica gel eluting with 1:1 hexanes:ethyl acetate. Removal of solvent gave the crude product as a single diastereomer (>25:1 ds) by ^1H NMR. Chromatography (silica gel/7:1 hexanes:ethyl acetate) gave 79 mg (74%) of **13d** as a clear oil (single diastereoisomer by ^1H NMR). ^1H NMR (CDCl_3 , TMS): δ 7.40–7.25 (m, 5H, ArH), 7.12–7.00 (m, 6H, ArH), 6.90 (m, 2H, ArH), 6.83 (d, $J = 6.9$ Hz, 2H, ArH), 5.82–5.68 (m, 1H, H₂C=CH-), 5.76 (d, $J = 8.4$ Hz, 1H, PhC(O) H_{oxa}), 5.26–5.03 (m, 3H, C=CH₂ and PhC(N) H_{oxa}), 5.00 (d, $J = 12.3$ Hz, 1H, PhCH₂O), 4.87 (d, $J = 12.3$ Hz, PhCH₂O), 4.03 (dd, $J = 6.0, 9.9$ Hz, 1H, α -H), 3.11–3.00 (m, 1H, β -CHH), 2.83–2.75 (m, 1H, β -CHH), 1.63 (s, 3H, CH₃). ^{13}C NMR (CDCl_3): δ 169.5 (CO_{ester}), 158.1 (CO_{oxa}), 134.7, 133.8, 133.4, 128.6, 128.5, 128.3, 128.0, 127.99, 127.9, 127.8, 126.0, 118.6, 79.8, 67.1, 65.4, 56.3, 33.4. IR (NaCl, film): ν 1761 (both CO's) cm^{-1} . $[\alpha]_{\text{D}}^{25} = +116^\circ$ ($c = 1.2$, CHCl_3 , 25°C). Anal. Calcd for $\text{C}_{27}\text{H}_{25}\text{NO}_4$: C, 75.86; H, 5.89; N, 3.28. Found: C, 75.89; H, 6.00; N, 3.24.

13e. According to the general procedure 4(R),5(S)-4 (100 mg, 0.25 mmol), CuI (25 mg, 0.13 mmol), and freshly prepared (4-methoxyphenyl)magnesium bromide (0.50 mL, 0.5 mmol, 1 M in THF) were allowed to react in THF (4 mL) at -78°C for 120 min then at -10°C for 30 min. Methanol (100 μL) was added at -10°C , and the reaction was warmed to room temperature then passed through a plug of silica gel eluting with 1:1 hexanes:ethyl acetate. Removal of the solvent gave the crude product as a single diastereomer (>25:1) by ^1H NMR. Recrystallization from hexanes/methylene chloride gave 108 mg (86%) of **13e** as clear crystals, mp = 140°C . ^1H NMR (CDCl_3 , TMS): δ 7.38–7.31 (m, 5H, ArH), 7.14 (d, $J = 8.7$ Hz, 2H, ArH), 7.06–6.97 (m, 4H, ArH), 6.83–6.74 (m, 6H, ArH), 6.15 (bs, 1H, ArH), 5.62 (d, $J = 8.4$ Hz, 1H, PhC(O) H_{oxa}), 5.23 (d, $J = 8.4$ Hz, 1H, PhC(N) H_{oxa}), 5.17 (d, $J = 12.3$ Hz, 1H, PhCH₂O), 5.07 (d, $J = 12.3$ Hz, 1H, PhCH₂O), 3.84–3.77 (m, 2H, α -H and β -CHH), 3.80 (s, 3H, OCH₃), 3.27 (dd, $J = 8.7, 17.4$ Hz, 1H, β -CHH). ^{13}C NMR (CDCl_3): δ 169.7 (CO_{ester}), 158.8, 158.6, 135.1, 134.8, 132.7, 130.7, 129.3, 128.6, 128.4, 128.3, 128.1, 127.8, 127.6, 126.1, 113.9, 79.6, 67.4, 66.6, 58.9, 55.3, 33.8. IR (NaCl, film): ν 1761 (CO), 1739 (CO) cm^{-1} . $[\alpha]_{\text{D}}^{25} = +120^\circ$ ($c = 1.2$, CHCl_3 , 25°C). Anal. Calcd for $\text{C}_{32}\text{H}_{29}\text{NO}_4$: C, 75.72; H, 5.76; N, 2.76. Found: C, 75.72; H, 6.00; N, 2.71.

13f. According to the general procedure 4(R),5(S)-4 (100 mg, 0.25 mmol), CuI (24 mg, 0.13 mmol), and ((trimethylsilyl)methyl)magnesium chloride (0.31 mL, 0.31 mmol, 1.0 M in THF) were allowed to react in THF (4 mL) at -78°C for 2 h then at -10°C for 30 min. Methanol (100 μL) was added at -10°C , and the reaction was warmed to room temperature then passed through a plug of silica gel eluting with 1:1 hexanes:ethyl acetate. Removal of the solvent gave the crude product as a 12:1 mixture of diastereomers (by ^1H NMR). Chromatography (silica gel/7:1 hexanes:ethyl acetate) gave 100 mg (82%) (12:1 mixture of diastereomers by ^1H NMR) of **13f** as a clear oil. ^1H NMR (CDCl_3 ,

TMS): δ 7.40–7.24 (m, 5H, ArH), 7.11–7.00 (m, 6H, ArH), 6.95 (m, 2H, ArH), 6.84 (dd, $J = 1.2, 7.5$ Hz, 2H, ArH), 5.81 (d, $J = 8.4$ Hz, 1H, PhC(O) H_{oxa}), 5.12 (d, $J = 8.4$ Hz, 1H, PhC(N) H_{oxa}), 4.90 (d, $J = 12.3$ Hz, 1H, PhCH₂O), 4.77 (d, $J = 12.3$ Hz, 1H, PhCH₂O), 3.99 (dd, $J = 6.6, 8.4$ Hz, 1H, α -H), 2.16–2.01 (m, 2H, β -CH₂), 0.60 (dt, $J = 4.8, 13.8$ Hz, 1H, (TMS)CHH), 0.40 (dt, $J = 4.8, 13.2$ Hz, 1H, (TMS)-CHH), 0.00 (s, 9H, Si(CH₃)₃). ^{13}C NMR (CDCl_3): δ 169.9 (CO_{ester}), 158.0 (CO_{oxa}), 135.2, 134.7, 133.9, 128.5, 128.3, 128.2, 128.0, 127.8, 127.79, 126.0, 79.8, 66.8, 65.0, 59.5, 24.1, 13.4, -1.9. IR (NaCl, film): ν 1761 (both CO's) cm^{-1} . Anal. Calcd for $\text{C}_{29}\text{H}_{33}\text{NO}_4$: C, 71.43; H, 6.82; N, 2.87. Found: C, 71.56; H, 6.83; N, 2.83.

13g. According to the general procedure 4(R),5(S)-4 (100 mg, 0.25 mmol), CuI (24 mg, 0.13 mmol), and cyclohexylmagnesium chloride (0.20 mL, 0.40 mmol, 2.0 M in Et₂O) were allowed to react in THF (4 mL), at -78°C for 2 h then at 0°C for 30 min. Methanol (100 μL) was added at 0°C , and the reaction was warmed to room temperature and then passed through a plug of silica gel eluting with 1:1 hexanes:ethyl acetate. Removal of the solvent gave the crude product as a 9:1 mixture of diastereomers by ^1H NMR. Chromatography (silica gel/7:1 hexanes:ethyl acetate) gave 91 mg (75%) (single diastereoisomer by ^1H NMR) of **13g** as a clear oil. ^1H NMR (CDCl_3 , TMS): δ 7.37–7.26 (m, 5H, ArH), 7.11–7.00 (m, 6H, ArH), 6.95 (m, 2H, ArH), 6.84 (m, 2H, ArH), 5.81 (d, $J = 8.4$ Hz, 1H, PhC(O) H_{oxa}), 5.12 (d, $J = 8.4$ Hz, 1H, PhC(N) H_{oxa}), 4.99 (d, $J = 12.3$ Hz, 1H, PhCH₂O), 4.86 (d, $J = 12.6$ Hz, 1H, PhCH₂O), 4.05 (dd, $J = 6.3, 9.3$ Hz, 1H, α -H), 2.16 (ddd, $J = 5.1, 9.3, 15.1$ Hz, 1H, β -CHH), 1.88 (ddd, $J = 6.3, 8.4, 14.4$ Hz, 1H, β -CHH), 1.70–0.87 (m, 11H, cyclohexyl H's). ^{13}C NMR (CDCl_3): δ 170.4 (CO_{ester}), 158.1 (CO_{oxa}), 135.2, 134.8, 133.8, 128.5, 128.47, 128.4, 128.3, 127.9, 127.8, 125.9, 79.6, 67.0, 65.5, 54.6, 36.5, 34.2, 33.4, 26.3, 26.2, 25.9. IR (NaCl, film): ν 1758 (both CO's) cm^{-1} . $[\alpha]_{\text{D}}^{25} = +69.5^\circ$ ($c = 2.4$, CH_2Cl_2 , 25°C). Anal. Calcd for $\text{C}_{31}\text{H}_{33}\text{NO}_4$: C, 76.99; H, 6.88; N, 2.90. Found: C, 77.04; H, 7.00; N, 2.89.

13h. According to the general procedure, 4(R),5(S)-4 (100 mg, 0.25 mmol), CuI (25 mg, 0.13 mmol), and freshly prepared 1-adamantylmagnesium bromide²⁷ (1.5 mL, 0.45 mmol, 0.5 M in Et₂O) were allowed to react in THF (4 mL) at -78°C for 105 min then at room temperature for 30 min. Methanol (100 μL) was added, and the reaction was then passed through a plug of silica gel eluting with 1:1 hexanes:ethyl acetate. Removal of the solvent gave the crude product as a 4:1 mixture of diastereomers by ^1H NMR. Chromatography (silica gel/10:1 hexanes:ethyl acetate) gave 100 mg (75%) (6:1 mixture of diastereoisomers by ^1H NMR) of **13h** as a white solid (mp = 189°C). ^1H NMR (CDCl_3 , TMS): δ 7.33 (m, 5H, ArH), 7.25 (m, 2H, ArH), 7.09–6.95 (m, 8H, ArH), 6.85 (m, 2H, ArH), 5.79 (d, $J = 8.1$ Hz, 1H, PhC(O) H_{oxa}), 5.10 (d, $J = 8.1$ Hz, PhC(N) H_{oxa}), 4.74 (d, $J = 12.6$ Hz, 1H, PhCH₂O), 4.55 (d, $J = 12.3$ Hz, 1H, PhCH₂O), 4.46 (ap t, $J = 6.6$ Hz, 1H, α -H), 2.05 (dd, $J = 6.9, 14.4$ Hz, 1H, β -CHH), 1.89 (bs, 3H, adamantyl methines), 1.76–1.40 (m, 13H, β -CHH and adamantyl methylenes). ^{13}C NMR (CDCl_3): δ 170.1 (CO_{ester}), 157.6 (CO_{oxa}), 135.1, 134.4, 133.9, 128.5, 128.4, 128.2, 128.0, 127.9, 127.8, 126.0, 80.0, 66.8, 64.1, 52.1, 43.4, 42.1, 36.7, 32.1, 28.1. IR (NaCl, film): ν 1749 (both CO's) cm^{-1} . Anal. Calcd for $\text{C}_{35}\text{H}_{37}\text{NO}_4$: C, 78.48; H, 6.96; N, 2.62. Found: C, 78.56; H, 7.05; N, 2.62.

13i. According to the general procedure, 4(R),5(S)-4 (100 mg, 0.25 mmol), CuI (24 mg, 0.13 mmol), and isopropylmagnesium chloride (0.19 mL, 0.38 mmol, 2.0 M in Et₂O) were reacted in THF (4 mL) at -78°C for 100 min then at -10°C for 30 min. Methanol (100 μL) was added at -10°C , and the reaction was warmed to room temperature and then passed through a plug of silica gel eluting with 1:1 hexanes:ethyl acetate. Removal of the solvent gave the crude product as a 9:1 mixture of diastereomers (by ^1H NMR). Chromatography (silica gel/8:1 hexanes:ethyl acetate) gave 99 mg (84%) (10:1 mixture of diastereoisomers by ^1H NMR) of **13i** as a white solid, mp = 109°C . ^1H NMR (CDCl_3 , TMS): δ 7.39–7.24 (m, 5H, ArH), 7.09–6.99 (m, 6H, ArH), 6.93 (m, 2H, ArH), 6.83 (dd, $J = 1.5, 6.6$ Hz, 2H, ArH), 5.79 (d, $J = 8.7$ Hz, 1H, PhC(O) H_{oxa}), 5.11 (d, $J = 8.4$ Hz, PhC(N) H_{oxa}), 4.95 (d, $J = 12.3$ Hz, 1H, PhCH₂O), 4.81 (d, $J = 12.3$ Hz, 1H, PhCH₂O), 4.07 (dd, $J = 6.3, 9.3$ Hz, 1H, α -H), 2.13 (ddd, $J = 5.4, 9.0, 15.9$ Hz, 1H, β -CHH), 1.86 (ddd, $J = 6.3, 8.4, 14.4$ Hz, 1H, β -CHH), 1.72–1.63 (m, 1H, CHMe₂), 0.88 (d, $J = 7.2$ Hz, 3H, CH₃), 0.75 (d, $J = 6.6$ Hz, 3H, CH₃). ^{13}C NMR (CDCl_3): δ 170.3 (CO_{ester}), 158.1 (CO_{oxa}), 135.2, 134.7, 133.8, 128.5, 128.49, 128.4, 128.2, 128.0, 127.9, 127.8, 125.9, 79.6, 66.9, 65.2, 55.2, 38.1, 24.9, 22.8, 21.7. IR (NaCl, film): ν 1758 (both CO's) cm^{-1} . Anal. Calcd for $\text{C}_{28}\text{H}_{29}\text{NO}_4$: C, 75.82; H, 6.59; N, 3.16. Found: C, 75.61; H, 6.75; N, 3.12.

General Procedure for Formation/Purification of 14a–g. Pearlman's catalyst ($\text{Pd}(\text{OH})_2$ on carbon) was added to a solution of **13** in methanol/THF under a positive flow of argon. The mixture was then purged with H_2 four times followed by pressurizing to 60 psi of H_2 . The reaction was stirred for the indicated time and subsequently filtered through Celite with the aid of methanol to remove the catalyst. HCl (1 N) in ethanol was added to the filtrate, and the volatiles were removed by rotary evaporation. The resulting material was then triturated with dry diethyl ether (3X) to give the HCl salt of the amino acid. The neutral amino acid was obtained by ion exchange chromatography according to the following procedure: A slurry of Dowex 50X8–100 ion-exchange resin (approximately 1 g of resin/10 mg of HCl salt to be purified) in 2 N HCl (aq) was placed in a flash column and washed with distilled H_2O until the eluent was neutral (pH 7). The amino acid HCl salt was neutralized (pH 7) with 1.5% NH_4OH (aq) then applied to the column. Distilled H_2O (4–6 void volumes) was eluted through the resin, followed by elution with 1.5% NH_4OH (aq). Fractions were collected and those containing the amino acid (TLC: $\text{SiO}_2/4:1$ MeOH: H_2O , visualized with ninhydrin, $R_f = 0.7$ – 0.85) were lyophilized, giving the pure amino acid.

14a. According to the general procedure, **13a** (100 mg, 0.22 mmol) and $\text{Pd}(\text{OH})_2/\text{C}$ (90 mg, 0.13 mmol) were allowed to react in methanol/THF (4 mL/2 mL) under H_2 (60 psi) for 20 h. The reaction was filtered through Celite, and 0.5 mL of 1 N HCl was added to the filtrate. Removal of the volatiles and subsequent trituration with Et_2O gave the crude HCl salt. Ion-exchange chromatography gave 29 mg (90%) of the **14a**²⁸ as a white solid (89% ee). ^1H NMR (D_2O): δ 3.55 (dd, $J = 5.1, 7.5$ Hz, 1H, α -H), 1.77 (dd, $J = 4.8, 15.0$ Hz, 1H, β -CHH), 1.46 (dd, $J = 7.2, 15.0$ Hz, 1H, β -CHH), 0.82 (s, 9H, C(CH₃)₃). ^{13}C NMR (D_2O , CD_3OD): δ 176.8 (CO), 53.8, 45.8, 30.6, 29.5. IR (KBr): ν 1618, 1575, 1508 cm^{-1} . $[\alpha]_D = +7.0$ ($c = 0.5$, H_2O , 25 °C). Anal. Calcd for $\text{C}_7\text{H}_{15}\text{NO}_2$: C, 57.90; H, 10.41; N, 9.61. Found: C, 58.00; H, 10.29; N, 9.61.

14b. According to the general procedure, **13b** (119 mg, 0.23 mmol) and $\text{Pd}(\text{OH})_2/\text{C}$ (110 mg, 0.16 mmol) were allowed to react in methanol/THF (4 mL/1 mL) under H_2 (60 psi) for 19 h. The reaction was filtered through Celite, and 1 mL of 1 N HCl was added to the filtrate. Removal of the volatiles and subsequent trituration with Et_2O gave the crude HCl salt. Ion exchange chromatography gave 43 mg (89%) of the **14b** as a white solid (>98% ee). ^1H NMR (HCl salt in D_2O): δ 7.09–6.91 (m, 3H, ArH), 3.98 (dd, $J = 6.1, 9.1$ Hz, 1H, α -H), 3.25 (dd, $J = 6.2, 14.5$ Hz, 1H, β -CHH), 2.92 (dd, $J = 9.1, 14.5$ Hz, 1H, β -CHH), 2.67–2.56 (m, 4H, ArCH₂ × 2), 1.70–1.61 (m, 4H, –CH₂CH₂–). ^{13}C NMR (D_2O , CD_3OD): δ 172.6 (CO), 139.7, 137.1, 133.5, 130.1, 128.5, 126.8, 54.1, 34.2, 30.5, 26.7, 23.8, 23.2. IR (KBr): ν 1736, 1718 cm^{-1} . $[\alpha]_D = -1.0$ ($c = 0.8$, 4% HCl , 26 °C). High-resolution mass measurement calcd for $\text{C}_{13}\text{H}_{17}\text{NO}_2$ 219.1259, found 219.1256.

14c. According to the general procedure **13c** (75 mg, 0.17 mmol) and $\text{Pd}(\text{OH})_2/\text{C}$ (70 mg, 0.10 mmol) were allowed to react in methanol/THF (3 mL/2 mL) under H_2 (60 psi) for 10 h. The reaction was filtered through Celite, and 0.5 mL of 1 N HCl was added to the filtrate. Removal of the volatiles and subsequent trituration with Et_2O gave the crude HCl salt. Ion-exchange chromatography gave 20 mg (90%) of the **14c**²⁸ as a white solid (88% ee). ^1H NMR (D_2O): δ 3.55 (ap t, $J = 6.8$ Hz, 1H, α -H), 1.56–1.51 (m, 3H, β -CH₂ and CHMe₂), 0.80 (d, $J = 3.3$ Hz, 3H, CH₃), 0.78 (d, $J = 3.3$ Hz, 3H, CH₃). ^{13}C NMR (D_2O , CD_3OD): δ 176.3 (CO), 54.4, 40.9, 25.2, 23.0, 21.8. IR (KBr): ν 1622, 1574, 1509 cm^{-1} . $[\alpha]_D = +6.9$ ($c = 0.54$, H_2O , 26 °C).

14d. According to the general procedure, **13d** (80 mg, 0.19 mmol) and $\text{Pd}(\text{OH})_2/\text{C}$ (75 mg, 0.11 mmol) were allowed to react in methanol/THF (4 mL/1 mL) under H_2 (60 psi) for 10.5 h. The reaction was filtered through Celite, and 0.5 mL of 1 N HCl was added to the filtrate. Removal of the volatiles and subsequent trituration with Et_2O gave the crude HCl salt. Ion-exchange chromatography gave 20 mg (91%) of the **14d**²⁸ as a white solid (92% ee). ^1H NMR (D_2O): δ 3.57 (ap t, $J = 6.3$ Hz, 1H, α -H), 1.72–1.60 (m, 2H, β -CH₂), 1.30–1.17 (m, 2H, γ -CH₂), 0.79 (t, $J = 7.2$ Hz, 3H, CH₃). ^{13}C NMR (D_2O , CD_3OD): δ 175.9 (CO), 55.7, 33.6, 18.9, 13.9. IR (KBr): ν 1655, 1627, 1583 cm^{-1} . $[\alpha]_D = -1.7^\circ$ ($c = 0.6$, H_2O , 26 °C).

14e. According to the general procedure, **13e** (108 mg, 0.21 mmol), $\text{Pd}(\text{OH})_2/\text{C}$ (100 mg, 0.14 mmol) were reacted in methanol/THF (3 mL/2 mL) under H_2 (60 psi) for 15 h. The reaction was filtered through Celite, and 0.5 mL of 1 N HCl was added to the filtrate. Removal of the volatiles and subsequent trituration with Et_2O gave the crude HCl salt. Ion-exchange chromatography gave 38 mg (93%) of the **14e** as a white solid (97% ee). ^1H NMR (D_2O): δ 7.11 (d, $J = 8.4$ Hz, 2H, ArH),

6.85 (d, $J = 8.4$ Hz, 2H, ArH), 3.79 (dd, $J = 5.4, 7.5$ Hz, 1H, α -H), 3.68 (s, 3H, –OCH₃), 3.07 (dd, $J = 5.4, 14.7$ Hz, 1H, β -CH₂), 2.90 (dd, $J = 7.8, 14.7$ Hz, 1H, β -CH₂). ^{13}C NMR (67.9 MHz, Bruker WP-270) (D_2O , CD_3OD): δ 174.8 (CO), 159.3, 142.6, 131.6, 128.6, 115.5, 57.1, 56.3, 36.5. IR (KBr): ν 1617, 1587 cm^{-1} . HCl salt: $[\alpha]_D = +27.5$ ($c = 0.51$, H_2O , 26 °C).

14f. According to the general procedure, **13f** (100 mg, 0.21 mmol) and $\text{Pd}(\text{OH})_2/\text{C}$ (90 mg, 0.13 mmol) were allowed to react in methanol/THF (3 mL/2 mL) under H_2 (60 psi) for 10 h. The reaction was filtered through Celite, and 0.5 mL of 1 N HCl was added to the filtrate. Removal of the volatiles and subsequent trituration with Et_2O gave the crude HCl salt. Ion-exchange chromatography gave 34 mg (97%) of the **14f** as a white solid (88% ee). ^1H NMR (CD_3OD): δ 3.50 (ap t, $J = 6.0$ Hz, 1H, α -H), 1.91–1.81 (m, 2H, β -CH₂), 0.60–0.55 (m, 2H, CH₂(TMS)), 0.02 (s, 9H, Si(CH₃)₃). ^{13}C NMR (CD_3OD): δ 174.4 (CO), 59.4, 26.9, 12.3, –1.9. IR (KBr): ν 1603, 1508 cm^{-1} . $[\alpha]_D = -3.4^\circ$ ($c = 0.35$, MeOH, 25 °C). Anal. Calcd for $\text{C}_7\text{H}_{17}\text{NO}_2\text{Si}$: C, 47.96; H, 9.77; N, 7.99. Found: C, 47.78; H, 9.52; N, 7.90.

14g. According to the general procedure, **13g** (90 mg, 0.18 mmol) and $\text{Pd}(\text{OH})_2/\text{C}$ (85 mg, 0.12 mmol) were allowed to react in methanol/THF (3 mL/2 mL) under H_2 (60 psi) for 24 h. The reaction was filtered through Celite, and 1.0 mL of 1 N HCl was added to the filtrate. Removal of the volatiles and subsequent trituration with Et_2O gave the crude HCl salt. Ion-exchange chromatography gave 30 mg (98%) of the **14g**²⁸ as a white solid (97% ee). ^1H NMR (D_2O): δ 3.59 (dd, $J = 5.4, 8.7$ Hz, 1H, α -H), 1.60–1.45 (m, 8H, β -CH₂ and cyclohexyl H's), 1.23–0.78 (m, 5H, cyclohexyl H's). ^{13}C NMR (D_2O , CD_3OD): δ 176.4 (CO), 53.7, 39.4, 34.4, 34.0, 32.8, 26.9, 26.6, 26.5. IR (KBr): ν 1624, 1586 cm^{-1} . $[\alpha]_D = -2.5^\circ$ ($c = 0.2$, H_2O , 25 °C). Anal. Calcd for $\text{C}_9\text{H}_{17}\text{NO}_2$: C, 63.13; H, 10.01; N, 8.18. Found: C, 63.07; H, 9.89; N, 7.96.

14h. According to the general procedure, **13h** (92 mg, 0.17 mmol) and $\text{Pd}(\text{OH})_2/\text{C}$ (80 mg, 0.11 mmol) were allowed to react in methanol/THF (2 mL/2 mL) under H_2 (60 psi) for 13 h. The reaction was filtered through Celite, and 1.0 mL of 1 N HCl was added to the filtrate. Removal of the volatiles and subsequent trituration with Et_2O gave the crude HCl salt. Ion-exchange chromatography gave 30 mg (97%) of the **14h**²⁸ as a white solid (73% ee). ^1H NMR (HCl salt in CD_3OD): δ 3.90 (bs, 1H, α -H), 1.99 (bs, 3H, adamantyl methines), 1.79–1.56 (m, 14H, β -CH₂ and adamantyl methylenes). ^{13}C NMR of HCl salt (CD_3OD): δ 174.2 (CO), 50.2, 46.0, 42.5, 37.3, 32.9, 29.4. IR (KBr): ν 1745, 1636 cm^{-1} . $[\alpha]_D = -11.4^\circ$ ($c = 0.7$, MeOH, 25 °C).

Compound 15. Boron trifluoride etherate (34 μL , 0.28 mmol) was added to a solution of racemic **5** (100 mg, 0.25 mmol) in benzene (2.5 mL) under argon at room temperature, and the resulting mixture was stirred for 20 min. Furan (72 μL , 1.0 mmol) was then added, and the reaction was stirred an additional 8 h. Filtration of the reaction mixture through silica gel using 1:1 hexanes:ethyl acetate as the eluent gave 117 mg (quantitative) of **15** as an oil and a single diastereoisomer by ^1H NMR. Chromatography ($\text{SiO}_2/5:1$ hexane:EtOAc) gave 105 mg (90%) of **15**. ^1H NMR (CDCl_3 , TMS): δ 7.37–7.31 (m, 5H, ArH), 7.24 (m, 1H, 5-furyl H), 7.05–6.90 (m, 8H, ArH), 6.67 (br s, 2H, ArH), 6.16 (dd, 1H, $J = 3.3, 1.8$ Hz, furyl H), 6.07 (dd, 1H, $J = 3.5, 0.8$ Hz, furyl H), 5.91 (d, 1H, $J = 8.4$ Hz, PhCHO), 5.30 (d, 1H, $J = 12.3$ Hz, PhCH₂O), 5.26 (d, 1H, $J = 12.6$ Hz, PhCH₂O), 4.86 (d, 1H, $J = 8.4$ Hz, PhCHN), 1.93 (s, 3H, CH₃). ^{13}C NMR (CDCl_3): δ 169.5 (CO_{ester}), 157.2 (CO_{oxa}), 149.5, 142.8, 135.8, 135.4, 134.4, 128.5, 128.2, 128.1, 127.8, 127.7, 127.6, 127.5, 127.4, 125.9, 110.8, 110.5, 80.3, 68.00, 64.8, 61.8, 20.7. IR (NaCl, film): ν 1752 cm^{-1} . Anal. Calcd for $\text{C}_{29}\text{H}_{25}\text{NO}_5$: C, 74.50; H, 5.39; N, 3.00. Found: C, 74.35; H, 5.41; N, 2.94.

General Procedure for the Preparation of Mosher Amides. The amino acid (1 equiv), Mosher acid chloride (1 equiv), and propylene oxide (4 equiv) were heated at reflux in THF for 45–60 min. After cooling, the solvent was removed from the reaction mixture *in vacuo*, yielding the Mosher amide as an oil. The % ee's were determined by examination of the ^{19}F NMR of the Mosher amides of the optically active amino acids and comparison to the corresponding Mosher amides of the racemic amino acids. The racemic amino acids were synthesized in the same manner as the optically active series.

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