Allylboration of α-Amino Ketones

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Received February 10, 1995[⊗]

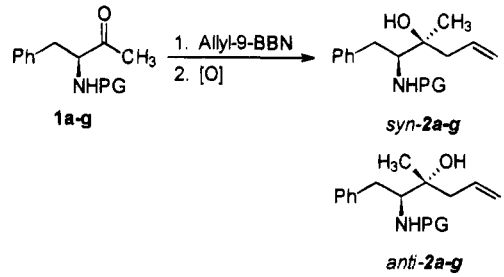
A series of unsaturated α-amino alcohols were prepared via the allylboration of the corresponding *N*-protected α-amino ketones. The reactions are stereoselective, producing the *syn* isomers. The diastereoselectivity is not dramatically effected by the electronic nature of the *N*-protecting group or the reaction temperature but is dependent on the steric requirements of the *N*-protecting group and the solvent system.

Introduction

Allyl- and crotylmetalations of aldehydes have proven to be valuable alternatives to conventional aldol methodology due to the high degree of stereoselection associated with these reactions.[1] Single and double asymmetric allylborations of aldehydes typically proceed with excellent levels of enantio- and diastereoselectivities.[2] Although the reaction of achiral and chiral allylboron reagents with α-substituted aldehydes has been investigated,[3] little attention has been directed toward the allylboration of chiral α-substituted ketones.[4] Yamamoto has reported the reaction of allyl-9-BBN with pyruvate esters in which the diastereoselectivity was shown to be dependent upon the steric bulk of the ester functionality.[4a] In an earlier study, we demonstrated that the allylborations of α-hydroxy ketones[5] and α-oxo carboxylic acids[6] using diisopropoxyallylborane proceeded with excellent diastereoselectivities, presumably via a rigid bicyclic transition state. To date, no report has appeared in the literature concerning the allylboration of α-amino ketones, although a few reports have appeared concerning the allylboration of α-amino aldehydes.[7]

We wish to report that allylborations of *N*-protected α-amino ketones using either allyl-9-BBN or diisopropoxyallylborane proceed with good *syn* diastereoselectivity (Scheme 1). Intramolecular hydrogen bonding between the NH proton and the ketone carbonyl of **1** plays a significant role in the stereoselectivity observed. We have found that the electronic nature of the *N*-protecting group (PG) has a minimal impact upon the stereochemical outcome. However, the *syn* diastereoselectivity increases with the increasing steric bulk of the PG. Reaction conditions also play an important role in controlling the diastereoselectivity.

Scheme 1



a: PG = BOC **e**: PG = *p*-Toluoyl
b: PG = Tos **f**: PG = 4-*t*-Butylbenzoyl
c: PG = Ac **g**: PG = 3,4-DMB
d: PG = Bz

Amino alcohol subunits are found in a wide variety of compounds that possess interesting and useful biological properties. Therefore, chiral unsaturated amino alcohols **2a–g** should find use as potential precursors to an extensive array of biologically important products. Indeed, the stereoselective synthesis of unsaturated amino alcohols via allylboration would comprise a direct route to intermediates involved in the synthesis of such compounds as statine,[8] bleomycin,[9] sibrosamine,[10] glycosphingolipids,[11] bestatine,[12] 3-methylstatine,[13] peptidase inhibitors,[14] HIV-1 protease inhibitors,[15] renin inhibi-

[⊗] Abstract published in *Advance ACS Abstracts,* July 1, 1995.

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Table 1. Stereochemical Effect of Various N-Protecting Groups[a]

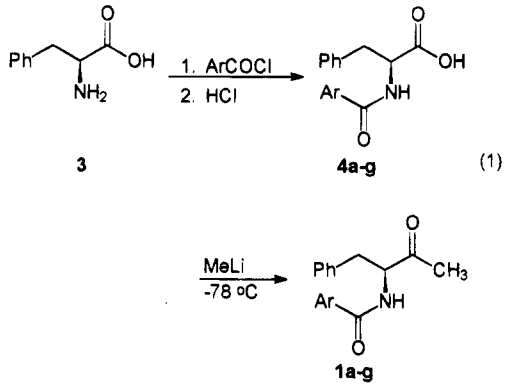
entry	ketone (PG)	product	% yield[b]	syn/anti	%de[c]	$-\Delta\Delta G^{\ddagger}$[d]
1	**1a** (Boc)	**2a**	80	80:20	60	0.82
2	**1b** (Tos)	**2b**	94	79:21	58	0.78
3	**1c**[e] (Ac)	**2c**[e]	80	80:20	60	0.82
4	**1d** (Bz)	**2d**	80	85:15	70	1.0
5	**1e** (*p*-Toluoyl)	**2e**	85	85:15	70	1.0
6	**1f** (4-*tert*-Butylbenzoyl)	**2f**	90	99:1	98	2.7
7	**1g** (3,4-DMB)	**2g**	90	88:12	76	1.2

[a] Reaction conditions: allyl-9-BBN added to equimolar quantity of ketone **1** in CH_2Cl_2 at 25 °C. [b] Isolated yields. [c] The de was determined by ^{1}H-NMR. Absolute configuration was determined by ^{13}C-NMR and 2D-NOE studies. [d] kcal/mol at 25 °C. [e] Racemic.

tors,[16] 3-methyl β-hydroxy-α-*N*-methylamino acid,[17] fumonisine B1,[18] and cathepsin D inhibitors.[19]

Results and Discussion

The direction of the intrinsic diastereoselectivity in the allylboration of *N*-protected α-amino ketones was examined with respect to optimization of the experimental factors controlling the diastereoselectivity.[20] α-Amino carbonyl compounds are generally not configurationally stable species due to their ready enolization.[21] Therefore, aroyl and sulfonyl *N*-protecting groups were used to eliminate this undesired reaction. All amino ketones were prepared by the addition of methyllithium to *N*-substituted amino acids.[22,23] In this study, ketones **1a–g** were chosen as the model substrates due to their straightforward preparation from readily available L-phenylalanine (eq 1).



Since the presence of an *N*-protecting group was requisite for suitable amino ketone stability, it was of interest to investigate its effect on the stereochemical outcome of the allylboration (Table 1). Changing the electronic nature of the *N*-protecting group did not drastically alter the product distribution (entries 1–5).

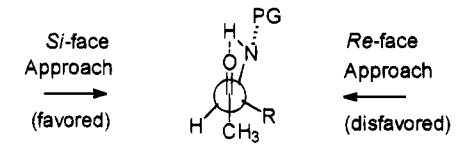


Figure 1.

There was a small but discernible effect when aroyl protecting groups were used (compare entries 1–3 with entries 4, 5, and 7). The sterically demanding 4-*tert*-butylbenzoyl group forced almost exclusive formation of the *syn*-diastereomer (entry 6). An intramolecularly hydrogen bonded amino ketone reasonably accounts for the stereochemical outcome as shown in Figure 1. In all cases, *si* face attack of the allylborane on the rotationally restricted ketone is energetically favored. Nonbonded interactions between the allylborane and the α-substituent destabilize *re* face attack which minimizes formation of the *anti* diastereomer. In studies involving α-alkoxy carbonyl compounds, where hydrogen bonding is not possible, the *anti* diastereomer predominates.[24] Disruption of the hydrogen bonding by solvent presumably allows for unrestricted rotation[25,26] about the C2–C3 bond in ketone **1**, which would provide the opportunity for stabilization of the *anti* selective transition state in a manner similar to the α-alkoxy carbonyl case (Figure 2).[27] Therefore, the reaction of **1d** with allyl-9-BBN in various solvents was investigated.

Indeed, the diastereoselectivity was significantly effected by the solvent (Table 2). The data clearly demonstrate that the $\Delta\Delta G^{\ddagger}$ is solvent dependent. In polar complexing solvents, the reaction is essentially stereorandom. This supports the postulation that Lewis basic solvents can destabilize the *syn*-selective transition state (Figure 1) by complexing with the NH proton, permitting the *anti*-selective transition state (Figure 2) to compete. In nonpolar solvents, *syn*-selectivity is maximized. Association of the allylborane and ketone **1** is maximized

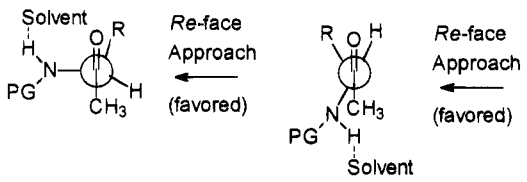


Figure 2.

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Table 2. Solvent Effects on the 2,3-*Syn* Selectivity (2d)[a]

entry	solvent	dielectric const., ϵ[135]	% de (25 °C)	$-\Delta\Delta G^{\ddagger}$,[b] kcal/mol
1	THF	7.58	4.0	0.047
2	Et_2O	4.34	46	0.59
3	CH_2Cl_2	9.08	70	1.0
4	toluene	2.38	82	1.4

[a] Reaction conditions: allyl-9-BBN added to equimolar quantity of ketone **1d** in solvent indicated. [b] $\Delta\Delta G^{\ddagger} = -RT \ln(\%syn/\%anti)$.

Table 3. *Syn* Selectivity at Various Temperatures (2d)[a]

		25 °C		0 °C		−78 °C	
entry	solvent	% de	$-\Delta\Delta G^{\ddagger}$	% de	$-\Delta\Delta G^{\ddagger}$	% de	$-\Delta\Delta G^{\ddagger}$
1	THF	4.0	0.047	4.0	0.043	6.0	0.047
2	Et_2O	46	0.59	68	0.90	66	0.61
3	CH_2Cl_2	70	1.0	84	1.3	88	1.1
4	toluene	82	1.4	82	1.3	86	1.0

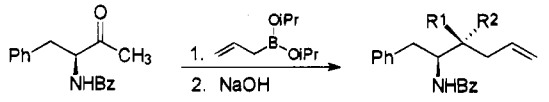
[a] Reaction conditions: allyl-9-BBN added to equimolar quantity of ketone **1d** in solvent indicated.

in nonpolar solvents, thus making nonbonded interactions between the allylborane and ketone more energetically significant. Further, the intramolecular hydrogen bond is stronger in nonpolar solvents. Interestingly, the difference in $\Delta\Delta G^{\ddagger}$ between entries 1 and 4 (Table 2) is about 1.4 kcal/mol, which approximates the strength of the hydrogen bond.

Reaction temperature also has an effect on the diastereoselectivity (Table 3). In all cases, the $\Delta\Delta G^{\ddagger}$ appears to be relatively independent of temperature. It is noteworthy that the largest temperature effects were observed in polar noncoordinating solvents (entry 3) and poorly coordinating solvents (entry 2).

Since allyl-9-BBN reacts instantaneously with **1**, a less reactive allylboration reagent was investigated. Dialkoxyallylboranes do not, generally, react with unsubstituted ketones.[5] However, α-heteroatom substituents activate ketones toward allylboration.[28] For example, in the reaction of lithium enolates with α-alkoxy carbonyl compounds, it was shown that the α-alkoxy substituents dramatically increased the rate of reaction through σ_I effects.[29]

As expected, diisopropoxyallylborane reacted completely with **1d** after 15 h at room temperature in methylene chloride (eq 2), providing a diastereomeric excess that was somewhat reduced (50% de) when compared to the reaction using allyl-9-BBN (70% de).



(2)

1d

syn-**2d**: R_1 = OH, R_2 = CH_3
anti-**2d**: R_1 = CH_3, R_2 = OH

Complexing diisopropoxyallylborane with DBU or triethylamine prior to reaction with **1d** resulted in an overall increase in the *syn*-selectivity, as shown in Table 4.

The observed increase in diastereoselectivity is significant (entry 1 versus entries 2 and 3). Presumably, the complexed allylboronate is too bulky to approach the hindered *re*-face of the intramolecularly hydrogen bonded

Table 4. Effect of Added Base on the Reaction of 1d with Diisopropoxyallylborane[a]

entry	Lewis base	rxn time, h	% de[b]	% yield (**2d**)
1	–	15	48	85
2	DBU	45	70	26
3	Et_3N	45	76	29

[a] Reaction conditions: equimolar quantity of allylboronic ester added to **1d** and base (if indicated) in CH_2Cl_2 at 25 °C. [b] In all cases, the *syn*-diastereomer predominated.

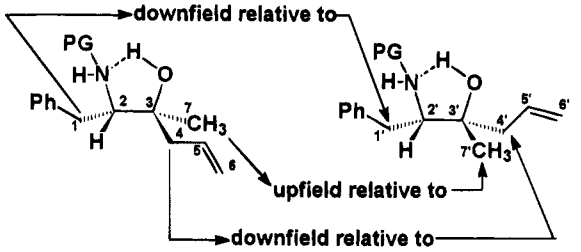
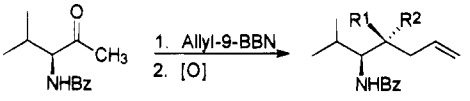


Figure 3.

α-amino ketone prior to the transfer of the allyl moiety (Figure 1). This forces the reagent to approach the less hindered face of the hydrogen bonded ketone **1d**. Apparently, the overall yield of **2d** is significantly reduced in the presence of DBU or Et_3N because the complexed allylboronate[6,9] must dissociate prior to allylboration.

Up to this point, only phenylalanine-derived ketones had been examined. Therefore, ketone **5** was allylborated using the standard conditions (eq 3). The valine-derived ketone **5** was chosen because of the greater bulkiness of the isopropyl group relative to the benzyl group in the phenylalanine derivatives. The ratio of *syn*-**6** to *anti*-**6** was significant, 94:6 in favor of the *syn* diastereomer. This important result, when compared to the data in Table 1, further supports the proposal that the allylation occurs at the least hindered, *si*-face of the α-amino ketone.



(3)

5

syn-**6**: R_1 = OH, R_2 = CH_3
anti-**6**: R_1 = CH_3, R_2 = OH

The absolute stereochemical outcome for each reaction was determined using NMR techniques. The product diastereomers were normally inseparable by column chromatography and Heathcock's ^{13}C-NMR correlation method was utilized to assign absolute stereochemistry.[30] The amino alcohol products constitute unique intramolecularly hydrogen bonded systems in which stereochemical assignments of the newly formed stereogenic center can readily be made. The basic principle of the Heathcock method, as applied to amino alcohols, is illustrated in Figure 3. The methyl group in the 2,3-*syn* diastereomer is shielded by the adjacent benzylic group and appears upfield relative to the sterically less congested 2,3-*anti* diastereomer's methyl group. The other carbons attached to either C(2) or C(3) are related to one another in a similar fashion. Table 5 provides a comparison of all allylborated compounds derived from the α-amino ketones.

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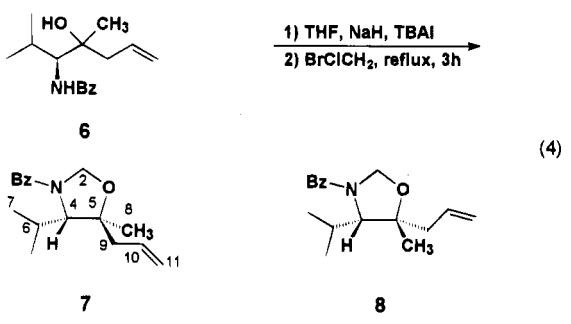
Table 5. ^{13}C-NMR Chemical Shifts of β-Amino Alcohols

		2,3-*Syn* (ppm)			2,3-*Anti* (ppm)		
entry	compound	C(4)	C(1)	C(7)	C(4′)	C(1′)	C(7′)
1	**2a**	44.64	35.75	23.85	44.23	35.44	24.36
2	**2b**	44.38	37.32	23.49	43.89	37.30	25.17
3	**2c**	44.99	35.31	23.89	44.19	35.01	25.11
4	**2d**	45.15	35.44	24.14	44.17	35.31	25.59
5	**2e**	45.20	35.40	24.12	44.21	35.28	25.62
6	**2f**	45.17	35.43	24.10	–	–	–
7	**2g**	45.21	35.39	24.06	44.19	35.19	29.76
8[a]	**6**	45.65	28.67	24.59	46.10	28.32	25.03

[a] The C(4)–C(4′) relationship is reversed in this case. However, the C(6)–C(6′) relationship of δ118.64/δ119.86 is as expected.

The correlation between the ^{13}C-NMR shifts and stereochemical orientations of groups about the C(2)–C(3) bond are precisely what the Heathcock model predicts for systems of this type. Note that C(1) always appears downfield C(1′). Likewise, except in one case (entry 8), C(4) is deshielded relative to C(4′). Finally, the diastereomeric methyl groups consistently exhibit a shielding pattern in which C(7) is shielded relative to C(7′). This method has been used extensively as a method for assigning absolute configurations to newly created stereogenic centers contained within β-hydroxy ketones and 1,2-diols.[31]

The absolute configuration of *syn*-**6** was confirmed by ROESY analysis of the ring locked product (eq 4). The syntheses of the azoxiranes were carried out according to a procedure reported by Burgess.[32] Repeated attempts resulted in the isolation of only one diastereomer, **7**. ROESY analysis revealed a strong correlation between



6 (4)

7 **8**

the H_7 methyl protons and H_8 methyl protons. Further, a correlation was shown to exist between the H_6 and H_8 protons. Based on the yield of compound **7**, it was concluded that it resulted from the major *syn*-diastereomer.

Conclusion

The chemistry described in this paper demonstrates that the allylboration of *N*-protected α-amino ketones can be achieved with either dialkyl- or dialkoxyallylboranes in excellent yields and good diastereoselectivities. The intrinsic diastereoselectivity is *syn* which appears to be a consequence of a transition state involving intramolecular hydrogen bonding. Further, the selectivity appears to be a function of the minimization of nonbonded interactions between the rotationally restricted *N*-protected α-amino ketone and the allylboron reagent. The reaction solvent plays a major role in the diastereoselectivity but reaction temperature has a minimal impact on the stereochemical outcome. Maximum diastereoselectivities are obtained using bulky *N*-protecting groups such as the 4-*tert*-butylbenzoyl derivative in noncomplexing solvents like methylene chloride and toluene.

Experimental Section

All melting points are uncorrected and were recorded using a MEL-TEMP melting point apparatus equipped with a Glas-Col digital thermometer. Optical rotations were measured on a Perkin-Elmer 241 Polarimeter. All ^{1}H- and ^{13}C-NMR spectra were recorded on a 250 MHz Bruker AC250 Spectrometer. Elemental analyses were performed by Atlantic Microlab, Norcross, GA. High resolution mass spectroscopy was performed by The University of Tennessee Center for Mass Spectroscopy. All glassware, syringes, and needles were dried at 250 °C for 12 h prior to use. All solvents were distilled prior to use.[33] Reactions were magnetically stirred and monitored by TLC. Solvents were removed under water-aspirated vacuum with a rotary evaporator unless otherwise indicated. Products were purified by flash chromatography using 230–400 mesh ASTM 60 Å silica gel.[34] Allyl-9-BBN,[35a] diisopropoxyallylborane,[35b] *N*-(*tert*-butoxycarbonyl)-L-phenylalanine (**4a**),[36] *N*-(*p*-toluenesulfonyl)-L-phenylalanine (**4b**),[22b] *N*-benzoyl-L-phenylalanine (**4d**),[22a] *N*-benzoyl-L-valine,[22a] and *N*-acetyl-4-phenyl-2-butanone (**1c**)[37] were prepared according to published procedures. *N*-Acetyl-L-phenylalanine (**4c**, Aldrich Chemical Co.) was used as received.

The amino alcohol diastereomers could not be separated by flash chromatography. All physical and spectral data are given based on the diastereomeric mixtures. Only the diastereotopic carbinol methyl groups are distinguishable by ^{1}H-NMR. The ^{13}C-NMR spectra provide information concerning the chemical shift differences between the diastereotopic carbons.

***N*-(*p*-Toluoyl)-L-phenylalanine (4e).** To a solution of L-phenylalanine (4.00 g, 24.2 mmol) in sodium hydroxide (15.0 mL, 2.0 N) cooled to 0 °C by means of an ice–water bath were alternately added toluoyl chloride (4.11 g, 26.6 mmol) and sodium hydroxide (15.0 mL, 2.0 N) in ten portions. The pH was checked after each cycle to insure that the reaction remained basic. Upon completion of the additions, the reaction mixture was stirred at room temperature for 15 min. Subsequently, the reaction was recooled to 0 °C, and concentrated hydrochloric acid was added to adjust the pH to 2–3 which yielded a white precipitate. The mixture was stored at −10 °C for 2 h. The white solid was then filtered and washed with hydrochloric acid (2 × 50 mL, 1.0 N) and distilled water (2 × 50 mL) and placed in a vacuum oven overnight to dry (1 mmHg). The crude solid was recrystallized from 60% aqueous ethanol. The desired acid was isolated in a 95% yield: $[\alpha]^{21}_D$ = +17.0° (*l* = 0.100, *c* = 0.0100, $CHCl_3$); mp = 143.0–144.5 °C; ^{1}H-NMR ($CDCl_3$ w/TMS) δ 9.00–8.45 (br s, 1H), 7.59 (d, 2H, *J* = 8.15 Hz), 7.35–7.15 (m, 7H), 6.58 (d, 1H, *J* = 7.28 Hz), 5.15–5.00 (m, 1H), 3.37 (dd, 1H, *J* = 14.00, 5.57 Hz), 3.26

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(dd, 1H, J = 13.98, 5.79 Hz), 2.39 (s, 3H); ^{13}C-NMR ($CDCl_3$) δ 175.26, 167.78, 142.73, 135.78, 130.67, 130.39, 129.46, 128.81, 127.39, 127.20, 53.75, 37.41, 21.58. Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 72.00; H, 6.12; N, 4.88.

***N*-(4-*tert*-Butylbenzoyl)-L-phenylalanine (4f)** was prepared via an esterification[38] –recrystallization–saponification[39] sequence due to the difficulty in isolating pure *N*-*p*-*tert*-butylbenzoylated acid via the previous procedure. The crude acid **4f** (1.45 g, 4.46 mmol), prepared as previously described, was placed in a 100-mL round-bottom flask containing methanol (40 mL), and then concentrated sulfuric acid (1 mL) was slowly added. A reflux condenser with a drying tube was placed on the flask, and the reaction mixture was heated to reflux for 1 h. After cooling, the reaction mixture was diluted with water (25 mL) and extracted with diethyl ether (3 × 25 mL). The combined etheral extracts were washed with saturated sodium bicarbonate (1 × 50 mL) and placed over magnesium sulfate. The drying agent was removed by filtration, and the solvent was removed under reduced pressure to give a crystalline white solid.

Recrystallization using 20% ethyl acetate in hexanes gave an 82% yield of the desired ester: $[\alpha]^{24}_D$ = +94.9° (l = 0.100, c = 0.0193, $CHCl_3$); mp = 98.5–99 °C; ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.67 (d, 2H, J = 8.41 Hz), 7.43 (d, 2H, J = 8.44 Hz), 7.35–7.10 (m, 5 H), 6.58 (d, 1H, J = 7.35 Hz), 5.15–5.00 (m, 1H), 3.72 (s, 3H), 3.40–3.10 (m, 2H), 1.32 (s, 9H); ^{13}C-NMR ($CDCl_3$) δ 172.17, 166.80, 155.37, 136.02, 131.14, 129.42, 128.68, 127.23, 126.93, 125.82, 53.54, 52.42, 38.04, 35.01, 31.22.

Saponification was carried out as follows: to a stirred solution of the methyl ester (1.24 g, 3.66 mmol) in a 3:1 mixture of methanol:water (30 mL) in a 100-mL round-bottomed flask was added lithium hydroxide (0.175 g, 7.32 mmol). This mixture was stirred at room temperature for 15 h. Hydrochloric acid (2.0 N, ca. 10 mL) was added to make the reaction mixture slightly acidic. Extraction with diethyl ether (3 × 25 mL) followed by drying over magnesium sulfate, filtration, and solvent removal provided 90% of the desired acid, **4f**: $[\alpha]^{21}_D$ = +80.4° (l = 0.100, c = 0.0199, $CHCl_3$); mp = 160.1–161.0 °C; ^{1}H-NMR ($CDCl_3$ w/TMS) δ 9.30–8.90 (br s, 1H), 7.56 (d, 2H, J = 8.40 Hz), 7.34 (d, 2H, J = 8.42 Hz), 7.25–7.05 (m, 5H), 6.59 (d, 1H, J = 7.15 Hz), 5.10–4.90 (m, 1H), 3.40–3.10 (m, 2H), 1.22 (s, 9H); ^{13}C-NMR ($CDCl_3$) δ 175.06, 167.87, 155.79, 135.83, 130.59, 129.54, 128.81, 127.35, 127.08, 125.74, 53.78, 37.40, 35.07, 31.22. Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.28; H, 7.12; N, 4.30. Found: C, 73.17; H, 7.20; N, 4.27.

***N*-(3,4-Dimethoxybenzoyl)-L-phenylalanine (4g)** was also prepared via an esterification–saponification sequence as outlined for **4f** due to difficulty in isolating pure **4g**. Crude **4g** was synthesized via the procedure utilized for **4e** and then converted to the methyl ester in 68% yield: $[\alpha]^{24}_D$ = +62.7° (l = 0.100, c = 0.0750, $CHCl_3$); mp = 129.8–130.0 °C; ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.40–6.80 (m, 8H), 6.55 (d, 1H, J = 7.43 Hz), 5.15–5.02 (m, 1H), 3.91 (s, 6H), 3.78 (s, 3H), 3.35–3.15 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ 172.26, 166.47, 152.12, 149.12, 136.02, 129.42, 128.66, 127.24, 126.62, 119.62, 110.70, 110.44, 56.08, 53.58, 52.44, 38.03. Anal. Calcd for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16; N, 4.08. Found: C, 66.79; H, 5.97; N, 3.90.

Saponification according to the procedure outlined for **4f** gave a 95% yield of **4g**: $[\alpha]^{24}_D$ = +74.1° (l = 0.100, c = 0.0581, $CHCl_3$); mp = 160.5–160.8 °C; ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.41–6.80 (m, 8H), 6.46 (d, 1H, J = 7.07 Hz), 5.15–5.02 (m, 1H), 3.91 (s, 3H), 3.78 (s, 3H), 3.35–3.15 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ 174.90, 167.31, 152.46, 148.99, 136.01, 129.51, 128.74, 127.32, 126.00, 119.50, 110.72, 110.51, 56.08, 53.98, 37.50. Anal. Calcd for $C_{18}H_{19}NO_5$: C, 65.64; H, 5.81; N, 4.25. Found: C, 65.50; H, 5.86; N, 4.19.

(3*S*)-3-(*N*-Benzoylamino)-4-phenyl-2-butanone (1d). This procedure is general for all *N*-protected α-amino ketones. A three-necked 100-mL round-bottomed flask equipped with a low temperature thermometer and pressure-equalizing addition funnel sealed with a septum was flushed with argon and charged with **4d** (2.69 g, 10.0 mmol) and THF (10.0 mL). This solution was cooled to −78 °C using a dry ice–acetone bath. The addition funnel was charged with methyllithium in diethyl ether (22.9 mL, 1.40 M) and addition was begun to the well-stirred amino acid solution such that the internal temperature did not exceed −65 °C (approximately 1 mL/min). Upon completion of the addition, the reaction mixture was allowed to warm to room temperature and stirring was continued for an additional 2 h. In order to prevent racemization, the reaction mixture was poured into hydrochloric acid (50 mL, 1.0 N). Diethyl ether (50 mL) was added and the mixture was stirred at room temperature for 10 min. The aqueous layer was separated and extracted with diethyl ether (3 × 25 mL), and the combined organic extracts were dried over anhydrous magnesium sulfate. After filtration, the solvent was removed by rotary evaporation. Purification was achieved by flash chromatography using a 50 mm diameter column packed with 12 in. of silica gel and a solvent system of 4.5% methanol in chloroform to give a 61% yield of the desired material: $[\alpha]^{21}_D$ = +102° (l = 0.100, c = 0.0500, $CHCl_3$); mp = 138.2–139.0 °C; ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.72 (d, 2H, J = 9.73 Hz), 7.55–7.10 (m, 8H), 6.84 (d, 1H, J = 6.07 Hz), 5.10–5.00 (m, 1H), 3.35–3.15 (m, 2H), 2.25 (s, 3H); ^{13}C-NMR ($CDCl_3$) δ 206.19, 166.93, 135.93, 133.88, 131.87, 129.38, 128.83, 128.72, 127.33, 127.08, 60.01, 37.40, 28.15. Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.31; H, 6.41; N, 5.20.

(3*S*)-3-(*N*-(*tert*-Butoxycarbonyl)amino)-4-phenyl-2-butanone (1a) was prepared in a 72% yield according to the procedure outlined for **1d** using **4a**, except purification by flash chromatography was achieved using a 50 mm diameter column, 12 in. of silica gel, and 25% ethyl acetate in hexanes: $[\alpha]^{21}_D$ = 0.0° (d = 0.100, c = 0.0340, $CHCl_3$); mp = 75.0–75.8 °C; ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.35–7.10 (m, 5H), 5.15 (br s, 1H), 4.65–4.45 (m, 1H), 3.20–2.90 (m, 2H), 2.13 (s, 3H), 1.40 (s, 9H); ^{13}C-NMR ($CDCl_3$) δ 205.10, 136.27, 129.32, 128.75, 127.12, 80.05, 60.83, 37.68, 28.40. Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.42; H, 8.04; N, 5.32. Found: C, 68.28; H, 8.09; N, 5.37.

(3*S*)-4-Phenyl-3-(*N*-(*p*-toluenesulfonyl)amino)-2-butanone (1b) was prepared in a 74% yield according to the procedure outlined for **1d** using **4b**: $[\alpha]^{21}_D$ = +45.3° (d = 0.100, c = 0.0340, $CHCl_3$); mp = 107.0–107.7 °C; ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.58 (d, 2H, J = 8.27 Hz), 7.30–7.00 (m, 7H), 5.29 (d, 1H, J = 7.23 Hz), 4.20–4.05 (m, 1H), 3.10–2.85 (m, 2H), 2.42 (s, 3H), 2.05 (s, 3H); ^{13}C-NMR ($CDCl_3$) δ 205.90, 143.75, 136.67, 135.07, 129.79, 129.32, 128.84, 127.38, 127.14, 62.76, 38.41, 27.68, 21.60. Anal. Calcd for $C_{17}H_{19}NO_3S$: C, 64.33; H, 6.03; N, 4.41; S, 10.10. Found: C, 64.44; H, 6.03; N, 4.32; S, 10.16.

(3*S*)-3-(*N*-(*p*-Toluoyl)amino)-4-phenyl-2-butanone (1e) was prepared in a 59% yield according to the procedure outlined for **1d** using **4e**: $[\alpha]^{21}_D$ = +123° (l = 0.100, c = 0.510, $CHCl_3$); mp = 123.0–123.6 °C; ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.63 (d, 2H, J = 8.21 Hz), 7.35–7.10 (m, 7H), 6.82 (d, 1H, J = 6.56 Hz), 5.10–5.00 (m, 1H), 3.35–3.10 (m, 2H), 2.39 (s, 3H), 2.20 (s, 3H); ^{13}C-NMR ($CDCl_3$) δ 206.32, 166.82, 142.30, 135.96, 131.10, 129.32, 128.74, 128.48, 127.23, 127.05, 59.92, 37.31, 28.09, 21.49. Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.70; H, 6.78; N, 4.94.

(3*S*)-3-(*N*-(4-*tert*-Butylbenzoyl)amino)-4-phenyl-2-butanone (1f) was prepared in a 63% yield according to the procedure outlined for **1d** using **4g**: slightly yellow thick oil; $[\alpha]^{21}_D$ = +59.5° (l = 0.100, c = 0.0168, $CHCl_3$); ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.71–7.13 (m, 9H), 6.83 (d, 1H, J = 6.34 Hz), 5.10–5.00 (m, 1H), 3.35–3.14 (m, 2H), 2.22 (s, 3H), 1.32 (s, 9H); ^{13}C-NMR ($CDCl_3$) δ 206.34, 166.86, 155.79, 136.02, 130.59, 129.35, 128.78, 127.26, 126.93, 125.62, 59.94, 37.31, 35.01, 31.21, 28.08. Anal. Calcd for $C_{21}H_{25}NO_2$: C, 77.99; H, 7.79; N, 4.33. Found: C, 77.81; H, 7.67; N, 4.26.

(3*S*)-3-(*N*-(3,4-Dimethoxybenzoyl)amino)-4-phenyl-2-butanone (1g) was prepared in a 58% yield according to the procedure outlined for **1d** using **4g**: $[\alpha]^{21}_D$ = +104.4° (l = 0.100, c = 0.083, $CHCl_3$); mp = 143.8–144.1 °C; ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.40–6.82 (m, 8H), 6.80–6.69 (d, 1H, J =

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6.70 Hz), 5.10–4.95 (m, 1H), 3.92 (s, 6H), 3.35–3.15 (m, 2H), 2.22 (s, 3H); ^{13}C-NMR ($CDCl_3$) δ 206.38, 166.50, 152.15, 149.16, 136.02, 129.38, 128.81, 127.32, 126.63, 119.68, 110.66, 110.47, 60.023, 56.12, 37.41, 28.16. Anal. Calcd for $C_{19}H_{21}NO_4$: C, 69.60; H, 6.61; N, 4.27. Found: C, 69.46; H, 6.49; N, 4.24.

(3*S*)-3-(*N*-Benzoylamino)-4-methyl-2-pentanone (5) was prepared in a 20% yield according to the procedure outlined for **1d** using *N*-benzoyl-L-valine:[22a] $[\alpha]^{21}_D = +163°$ (d = 0.100, c = 0.0115, $CHCl_3$); mp = 107.0–107.5 °C; ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.85–7.40 (m, 5H), 6.82 (d, 1H, J = 7.57 Hz), 4.91 (dd, 1H, J = 8.33, 3.93 Hz), 2.45–2.31 (m, 1H), 2.30 (s, 3H), 1.09 (d, 3H, J = 6.81 Hz), 0.88 (d, 3H, J = 6.87 Hz); ^{13}C-NMR ($CDCl_3$) δ 206.95, 167.59, 134.29, 131.66, 128.59, 127.07, 63.36, 30.54, 28.28, 20.00, 16.93. Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.20; H, 7.81; N, 6.39. Found: C, 71.31; H, 7.85; N, 6.43.

Allylboration with *B*-Allyl-9-BBN. All Compounds were prepared in a fashion analogous to that presented for **2d**. The experimental data for compounds **2a–g** follow the general procedure.

2-(*N*-Benzoylamino)-3-methyl-1-phenylhex-5-en-3-ol (2d). This procedure is representative: A dry, three-necked 100-mL round bottomed flask equipped with a mercury bubbler was flushed with argon and charged with **1d** (0.543 g, 2.03 mmol) and methylene chloride (10 mL). Allyl-9-BBN in methylene chloride (2.32 mL, 0.92 M) was added dropwise via syringe at room temperature. Upon completion of the addition, the reaction was allowed to stir for 1 h. After oxidative workup using sodium perborate (6.96 mmol, 1.07 g), water (10 mL), and sodium hydroxide (2.03 mmol, 1.0 N) with stirring at room temperature for 2 h, the aqueous layer was separated and extracted with diethyl ether (3 × 30 mL). The combined organic portions were extracted with brine (1 × 50 mL) and placed over magnesium sulfate. After removing the drying agent by filtration, the solvent was removed under vacuum to give 0.730 g of crude product. Flash chromatography, using a 40 mm diameter column with 12 in. of silica gel and a solvent system of 5% methanol in chloroform, gave an 85:15 *syn*:*anti* ratio (70% de) of **2d** in 85% yield: $[\alpha]^{21}_D = -70.0°$ (l = 0.100, c = 0.0100 in $CHCl_3$); mp = 148.0–148.5 °C; the spectral data for the (2*S*,3*S*) diastereomer (*syn*-**2d**): ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.55–7.10 (m, 10H), 6.27 (d, 1H, J=8.62 Hz), 6.10–5.85 (m, 1H), 5.30–5.05 (m, 2H), 4.30–4.10 (m, 1H), 3.55 (s, 1H), 3.26 (dd, 1H, J=14.21, 3.92 Hz), 2.85 (dd, 1H, J=14.16, 10.92 Hz), 2.55–2.25 (m, 2H), 1.32 (s, 3H); ^{13}C-NMR ($CDCl_3$) δ 168.71, 138.67, 134.90, 133.81, 131.57, 129.14, 128.65, 128.60, 126.90, 126.61, 118.98, 74.62, 59.17, 45.15, 35.44, 24.14; the spectral data for the (2*S*,3*R*) diastereomer (*anti*-**2d**): ^{1}H-NMR δ 1.30 (3-methyl); ^{13}C-NMR δ 119.33, 44.17, 35.31, 25.59. Anal. Calcd for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.49; N, 4.53. Found: C, 77.54; H, 7.52; N, 4.52.

2-(*N*-(*tert*-Butoxycarbonyl)amino)-3-methyl-1-phenylhex-5-en-3-ol (2a) was prepared according to the procedure outlined for **2d** in an 80% yield (80:20 *syn*:*anti*, 60% de) from **1a** as a thick oil: spectral data for the (2*S*,3*S*) diastereomer (*syn*-**2a**): ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.30–7.12 (m, 5H), 6.05–5.80 (m, 1H), 5.25–5.10 (m, 2H), 4.75–4.60 (m, 1H), 3.82–3.60 (m, 1H), 3.19–3.04 (m, 2H), 2.97 (br s, 1H), 2.37–2.25 (m, 2H), 1.40–1.06 (m, 12H); ^{13}C-NMR ($CDCl_3$) δ 156.40, 138.87, 133.86, 129.19, 128.21, 126.08, 118.55, 79.26, 74.36, 58.99, 44.64, 35.75, 28.19, 23.85; spectral data for the (2*S*,3*R*) diastereomer (*anti*-**2a**): ^{13}C-NMR δ 156.16, 138.91, 129.56, 118.75, 79.35, 74.21, 60.08, 44.23, 35.44, 27.89, 24.36. Anal. Calcd for $C_{18}H_{27}NO_3$: C, 78.79; H, 8.91; N, 4.59. Found: C, 78.71; H, 8.84; N, 4.50.

3-Methyl-1-phenyl-2-(*N*-(*p*-toluenesulfonyl)amino)hex-5-en-3-ol (2b) was prepared according to the procedure outlined for **2d** in a 94% yield (80:20 *syn*:*anti*, 60% de) from **1b**: $[\alpha]^{21}_D = -26.3°$ (l = 0.100, c = 0.0803, $CHCl_3$); mp = 84.0–86.3 °C; spectral data for the (2*S*,3*S*) diastereomer (*syn*-**2b**): ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.35–6.80 (m, 9H), 6.10–5.85 (m, 1H), 5.35–5.05 (m, 2H), 4.81 (d, 1H, J = 8.00 Hz), 3.60–3.40 (m, 1H), 2.98 (m, 2H), 2.55–2.25 (m, 3H), 2.37 (s, 3H), 1.28 (s, 3H); ^{13}C-NMR ($CDCl_3$) δ 142.88, 137.51, 136.60, 133.47, 129.53, 129.12, 128.57, 126.87, 126.39, 118.84, 73.83, 63.00, 44.38, 37.32, 23.49, 21.52; spectral data for the (2*S*,3*R*) diastereomer (*anti*-**2b**): ^{1}H-NMR δ 1.31 (3-methyl); ^{13}C-NMR δ 133.60, 129.23, 126.77, 118.90, 74.21, 64.09, 43.89, 37.30, 25.17. Anal. Calcd for $C_{20}H_{25}NO_3S$: C, 66.76; H, 7.00; N, 3.89; S, 8.91. Found: C, 66.93; H, 7.06; N, 3.79; S, 8.94.

(±)-2-(*N*-Acetylamino)-3-methyl-1-phenylhex-5-en-3-ol (2c) was prepared according to the procedure outlined for **2d** in an 80% yield (80:20 *syn*:*anti*, 60% de) from **1c**: mp = 58.0–60.0 °C; spectral data for the (2*S*,3*S*) and (2*R*,3*R*) enantiomers (*syn*-**2c**): ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.31–7.10 (m, 5H), 6.05–5.75 (m, br s, 2H), 5.25–5.05 (m, 2H), 4.08–3.92 (m, 1H), 3.09 (dd, 1H, J = 14.2, 3.63 Hz), 2.68 (dd, 1H, J = 14.15, 11.1 Hz), 2.40–2.22 (m, 2H), 1.81 (s, 3H), 1.25 (s, 3H); ^{13}C-NMR ($CDCl_3$) δ 171.14, 138.75, 133.80, 129.05, 128.46, 126.44, 118.73, 74.38, 58.55, 44.99, 35.31, 23.89, 23.06; spectral data for the (2*S*,3*R*) and (2*R*,3*S*) enantiomers (*anti*-**2c**): ^{1}H-NMR δ 1.22 (3-methyl); ^{13}C-NMR δ 44.19, 35.07, 25.11. Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.76; N, 5.66. Found: C, 72.72; H, 8.61; N, 5.54.

2-(*N*-(*p*-Toluoyl)amino)-3-methyl-1-phenylhex-5-en-3-ol (2e) was prepared in a 95% yield (84:16 *syn*:*anti*, 69% de) from **1e** according to the procedure outlined for **2d**: $[\alpha]^{21}_D = -32.9°$ (l = 0.100, c = 0.0140, $CHCl_3$); mp = 150.0–150.8 °C; spectral data for the (2*S*,3*S*) diastereomer (*syn*-**2e**): ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.45–7.10 (m, 9H), 6.20 (d, 1H, J = 8.43 Hz), 6.15–6.05 (m, 1H), 5.30–5.05 (m, 2H), 4.25–4.05 (m, 1H), 3.20 (dd, 1H, J = 14.21, 3.84 Hz), 2.95–2.80 (dd, 1H, J = 14.18, 10.96 Hz), 2.43–2.20 (m, 2H), 2.35 (s, 3H), 1.32 (s, 3H); ^{13}C-NMR ($CDCl_3$) δ 168.71, 142.03, 138.79, 133.96, 131.63, 129.23, 129.17, 128.63, 126.95, 126.56, 118.80, 74.62, 59.31, 45.20, 35.40, 24.12, 21.46; spectral data for the (2*S*,3*R*) diastereomer (*anti*-**2e**): ^{1}H-NMR δ 1.26 (3-methyl); ^{13}C-NMR δ 128.93, 124.77, 119.32, 48.53, 44.21, 35.28, 30.00, 25.62. Anal. Calcd for $C_{21}H_{25}NO_2$: C, 77.99; H, 7.79; N, 4.33. Found: C, 77.85; H, 7.85; N, 4.15.

2-(*N*-(4-*tert*-Butylbenzoyl)amino)-3-methyl-1-phenylhex-5-en-3-ol (2f) was prepared according to the procedure outlined for **2d** in 87% yield (99:1 *syn*:*anti*, 98% de) from **1f**: −203.5° (l = 0.100, c = 0.00742, $CHCl_3$); mp = 41.3–42.0 °C; spectral data for the (2*S*,3*S*) diastereomer (*syn*-**2f**): ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.50–7.10 (m, 9H), 6.48 (d, 1H, J = 8.57 Hz), 6.10–5.90 (m, 1H), 5.20–5.00 (m, 2H), 4.30–4.15 (m, 1H), 3.20 (dd, 1H, J= 14.20, 3.60 Hz), 2.86 (dd, 1H, J = 14.08, 10.95), 2.40–2.30 (m, 2H), 1.30, 1.25 (s, s, 12H); ^{13}C-NMR ($CDCl_3$) δ 168.68, 155.04, 138.79, 133.93, 131.62, 129.14, 128.65, 126.80, 126.57, 125.53, 118.80, 74.66, 59.26, 45.17, 35.43, 34.96, 31.19, 24.10. Anal. Calcd for $C_{24}H_{31}NO_2$: C, 78.87; H, 8.55; N, 3.83. Found: C, 78.76; H, 8.49; N, 3.75.

2-(*N*-(3,4-Dimethoxybenzoyl)amino)-3-methyl-1-phenyl-1-hex-5-en-3-ol (2g). This compound was prepared according to the procedure outlined for **2d** in 80% yield (80:20 *syn*:*anti*, 60% de) from **1g**: $[\alpha]^{24}_D = -75.7°$ (l = 0.100, c = 0.0700, $CHCl_3$); mp = 250 °C dec; spectral data for the (2*S*,3*S*) diastereomer (*syn*-**2g**): ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.32–6.70 (m, 8H), 6.18 (d, 1H, J = 8.36 Hz), 6.10–5.85 (m, 1H), 5.25–5.00 (m, 2H), 4.20–4.05 (m, 1H), 3.88 (s, 3H), 3.82 (s, 3H), 3.21 (dd, 1H, J = 14.23, 3.72 Hz), 2.88 (dd, 1H, J = 14.16, 11.08 Hz), 2.45–2.30 (m, 2H), 1.35 (s, 3H); ^{13}C-NMR ($CDCl_3$) δ 168.48, 151.91, 149.03, 138.82, 133.97, 129.15, 128.66, 127.10, 126.59, 119.41, 118.77, 110.67, 110.37, 74.64, 59.43, 56.05, 45.21, 35.39, 24.06; spectral data for the (2*S*,3*R*) diastereomer (*anti*-**2g**): ^{1}H-NMR δ 1.28 (3-methyl); ^{13}C-NMR δ 44.19, 35.19, 29.76: HRMS calcd for $C_{22}H_{27}NO_4$: $(M + H)^+$ 370.20183, found 370.2005.

Preparation of 2d Using Diisopropoxyallylborane. A dry, 50-mL round-bottomed flask equipped with a mercury bubbler was charged with **1d** (0.268 g, 1.00 mmol) and methylene chloride (5 mL). Diisopropoxyallylborane in methylene chloride (1.0 mmol, 0.93 M) was added in one portion followed by vigorous stirring for 15 h at room temperature. Reaction progress was monitored by TLC (10% methanol in chloroform, silica gel plates). Sodium hydroxide (5.0 mL, 2.0 N) was added, and the resulting solution was stirred at room temperature for 1 h. The organic layer was separated and the aqueous layer extracted with methylene chloride (3 × 25 mL). The combined organic portions were dried over anhydrous magnesium sulfate. After removing the drying agent by filtration and the solvent by rotary evaporation, the crude solid

(0.33 g) was purified by flash chromatography (5% methanol in chloroform, 20 mm diameter column, 12 in. of silica gel) to give a 74:26 *syn:anti* ratio (48% de) of the desired product **2d** in a yield of 85%.

Preparation of 2d in the Presence of DBU. This synthesis was carried out according to the previous procedure except that DBU (0.152 g, 1.00 mmol) was first added to the solution of diisopropoxyallylborane. Purification provided a 85:15 *syn:anti* ratio (70% de) of the desired product (**2d**) in a 26% yield.

Preparation of 2d in the Presence of Et_3N. This synthesis was carried out according to the previous procedure except that triethylamine (0.101 g, 1.00 mmol) was used. Purification provided an 88:12 *syn:anti* ratio (76% de) of the desired product (**2d**) in a 49% yield.

2,4-Dimethyl-3-(*N*-benzoylamino)hept-6-en-4-ol (6) was prepared according to the experimental procedure outlined for **2d** in an 87% yield (94:6 *syn:anti*, 88% de) from **5**: spectral data for the (3*S*,4*S*) diastereomer (*syn*-**6**): ^{1}H-NMR ($CDCl_3$ w/ TMS) δ 7.83–7.79 (m, 2H), 7.54–7.41 (m, 3H), 6.60 (d, 1H, J = 9.95 Hz), 5.96–5.80 (m, 1H), 5.19–5.06 (m, 2H), 4.05 (dd, 1H, J = 10.06, 2.61 Hz), 2.34–2.18 (m, 3H), 1.96 (br s, 1H), 1.29 (s, 3H), 1.01 (superimposed doublets, 6H, J = 7.10 Hz); ^{13}C-NMR ($CDCl_3$) δ 167.92, 135.03, 133.35, 131.45, 128.68, 127.02, 119.86, 74.89, 58.88, 45.65, 28.67, 24.59, 22.28, 17.20; spectral data for the (3*S*,4*R*) diastereomer (*anti*-**6**): ^{1}H-NMR δ 1.26 (4–methyl); ^{13}C-NMR δ 167.45, 118.64, 46.10, 36.34, 29.76, 28.32, 25.03. Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.46; H, 8.71; N, 5.27.

Synthesis of (4*S*,5*S*)-3-*N*-Benzoyl-4-(2-propyl)-5-methyl-5-(3-propenyl)-1,3-oxazolidine (7). A dry, 50-mL, three-necked, round-bottomed flask equipped with a mercury bubbler and West condenser was purged with argon and charged with amino alcohol **6** (88 mg, 0.34 mmol) and tetrahydrofuran (15 mL). Sodium hydride (60% dispersion in oil, 24 mg, 1.0 mmol) and tetrabutylammonium iodide (ca. 10 mg) were added sequentially, and the reaction mixture was stirred at room temperature for 5 min. After addition of bromochloromethane (259 mg, 2.00 mmol), the reaction mixture was refluxed for 5 h using an oil bath. The reaction mixture was cooled to room temperature and quenched with diethyl ether (50 mL). After washing with water (2 × 50 mL), the ether solution was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography (20 mm diameter column, 8 in. of silica gel, and a solvent system of 12% ethyl acetate in hexanes) to give 20 mg (50%) of **7** as a viscous oil: ^{1}H-NMR ($CDCl_3$ w/TMS) δ 7.59–7.35 (m, 5H), 5.88–5.18 (m, 1H), 5.16–5.04 (m, 3H), 4.67 (d, 1H, J = 3.67 Hz), 4.34 (d, 1H, J = 4.05 Hz), 2.25–2.01 (m, 3H), 1.36 (s, 3H), 1.08 (superimposed doublets, 6H, J = 6.94, 6.86 Hz); ^{13}C-NMR ($CDCl_3$) δ 152.55, 136.47, 133.23, 131.08, 128.64, 127.32, 118.98, 79.92, 64.62, 44.38, 29.48, 22.79, 22.16, 19.92, 18.34. Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.56; H, 8.37; N, 5.09.

Acknowledgment. We wish to acknowledge financial support from the U.S. Department of Energy, Eastman Chemical Co., and the Robert H. Cole Foundation.

JO950274I