Asymmetric Synthesis of *Erythro* and *Threo* α-Substituted β-Amino Esters

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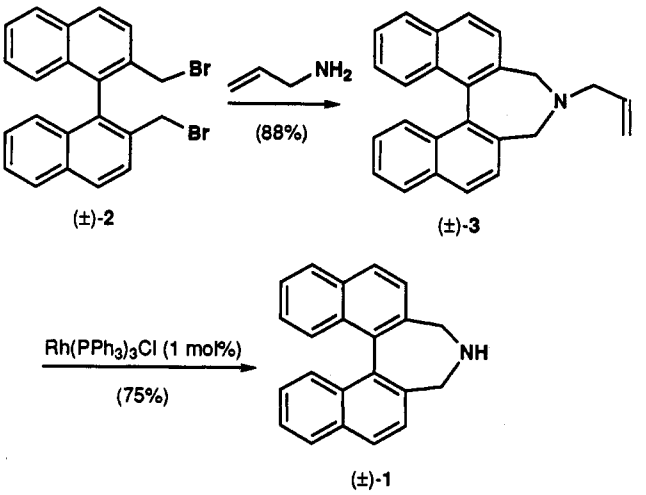
Received June 22, 1993

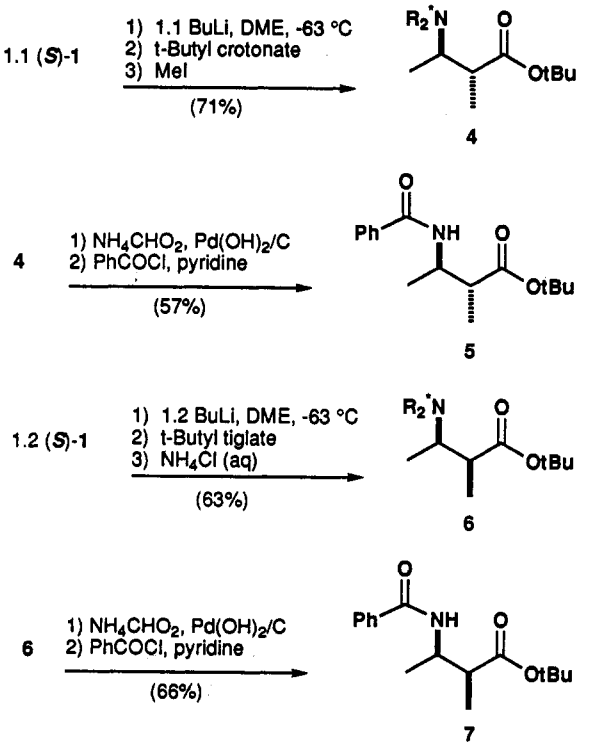
β-Amino esters are precursors for peptide components in active molecules,[1] β-lactams,[2] and other β-amino carbonyl compounds.[3] Most recently, a large amount of work has concerned the β-amino ester side chain of taxol.[4] We recently reported the asymmetric synthesis of β-amino esters using 3,5-dihydro-4*H*-dinaphth[2,1-c:1′,2′-*e*]azepine (**1**).[5] The enantiometrically pure lithium salt of **1** adds in a Michael sense to a variety of α,β-unsaturated esters in high yield with excellent diastereoselectivity.[6] Best results were obtained with *tert*-butyl esters in dimethoxyethane (DME) at −63 °C. Removal of the dimethylbinaphthyl moiety from the Michael adducts under reductive conditions gave deprotected β-amino esters with typically 95–99% ee. Here we report that the lithium enolates formed during the addition of lithiated **1** to α,β-unsaturated esters undergo stereoselective reactions with electrophiles; both *erythro* and *threo* β-amino esters have been prepared enantioselectively. A new synthesis of **1** which is more amenable to large scale is also described.

The published syntheses of **1**[7,8] start with (±)-2,2′-bis-(bromomethyl)-1,1′-binaphthyl (**2**)[9] and an ammonia synthon. We found the alkylation of 2,2,2-trifluoroacetamide[7] with **2** troublesome on a large scale due to reduced yields and the need for column chromatography. In contrast, slow addition of allylamine to **2** under dilute conditions gives tertiary amine **3**, which can be purified by trituration in acetone after filtration through a plug of silica gel (Scheme I). The allyl group of **3** is readily removed using Wilkinson's catalyst (1 mol %) in aqueous ethanol with concomitant azeotropic removal of propanal.[10] Over 60 g of racemic **1** has been made in one run. The published resolution of **1** has been scaled up to 20 g of racemic **1** successfully.[7] Asymmetric synthesis of **1** is a possibility, as **2** has been made enantioselectively.[11]

Scheme I



Scheme II



The addition of lithiated (*S*)-**1** to *tert*-butyl crotonate followed by the addition of methyl iodide to the intermediate enolate gave a 71% yield of Michael adduct **4** as a 65:2:2:1 mixture of diastereomers (Scheme II). This ratio was determined by HPLC, comparing **4** with an authentic mixture of the four diastereomers prepared by the addition of *tert*-butyl 3-amino-2-methylbutanoate (mixture of isomers) to (±)-**2**. The amine obtained by reductive removal of the dimethylbinaphthyl moiety from **4** was prone to β-elimination (as was **4**), thus it was protected with benzoyl chloride before isolation giving **5**.

To make the C-2 epimer of **5**, we envisioned adding lithiated (*S*)-**1** to *tert*-butyl tiglate and quenching the intermediate enolate with protic acid. The addition of

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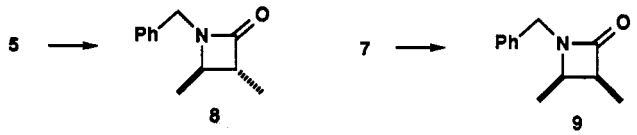
lithiated (*S*)-1 to the α-substituted α,β-unsaturated ester proceeded more slowly than for the unsubstituted ester. Using 1.2 equiv of the lithium amide and an elevated temperature (−63 °C to −46 °C), adduct 6 was produced in 63% yield as a 25:4:1:0 ratio of diastereomers. The major side product is isomer 4 (Scheme II). Better selectivity but lower yield was seen when the reaction was maintained at −63 °C. Removal of the dimethylbinaphthyl moiety and protection with benzoyl chloride gave amido ester 7.

The lithium amide and electrophile add *anti* across the carbon–carbon double bond of the ester in both cases. Yamamoto and co-workers obtained *anti* adducts in the racemic mode with the addition of lithium *N*-benzyl-*N*-(trimethylsilyl)amide to methyl crotonate followed by alkylation (*anti*/*syn* 52:48 to 89:11).[12] In our system, the major isomer from *tert*-butyl crotonate is the predominant minor product from *tert*-butyl tiglate, and visa versa. Earlier work showed that lithiated (*S*)-1 preferentially adds to the *re* face of *tert*-butyl crotonate, establishing the absolute stereochemistry at C-3 of 4 and 5[5]. Amido ester 5 was converted to β-lactam 8 [(1) BH_3;[13] (2) TFA; (3) 2-chloro-1-methylpyridinium iodide[14]]. The ^1H NMR



coupling constant between the protons at C-2 and C-3 (2 Hz) indicates that 8 is the *trans*-substituted lactam,[15a] establishing the stereochemistry at C-2 of 4 and 5. Diastereomerically pure 7 was similiarly converted to β-lactam 9. The ^1H NMR of 9 ($J_{\alpha,\beta}$ = 5.5 Hz) indicates that it is the *cis*-substituted lactam, establishing the 2,3-*syn* stereochemistry for 6 and 7. The optical rotation of 9 indicates that it has the absolute stereochemistry shown.[15b]

Our earlier work showed that lithiated 1 adds selectively to α,β-unsaturated *tert*-butyl esters with a variety of substituents at the β-carbon; these substituents can be bulky, oxygenated, and/or chiral.[5] Stereoselective quenching of the intermediate enolates with oxygen[16] or nitrogen[17] electrophiles, aldehydes,[18] or Michael acceptors[19] could lead to a number of molecules of current interest.[20]

Experimental Section

All reactions were conducted under an inert atmosphere. Dimethoxyethane (DME) was distilled from sodium/benzophenone, ethanol was distilled from sodium, and diethyl phthalate, triethylamine, and pyridine were distilled from tosyl chloride. Allylamine was distilled prior to use. α,β-Unsaturated esters were made using a literature procedure[21] and dried over molecular sieves. Palladium hydroxide on carbon (Pearlman's catalyst, 20% palladium, Aldrich)[22] was dried at 60 °C at 1 mmHg for 3 h before use. HPLC was performed on a 25-cm (10-mm i.d.) Regis Pirkle Type 1-A column and detected at 280 nm. Column chromatography was done using Kieselgel 60 230–400 mesh silica gel following procedure of Still et al.[23]

(±)-3,5-Dihydro-4-(3-propenyl)dinaphth[2,1-*c*:1′,2′-*e*]azepine (3). To 168.5 g (0.383 mol) of (±)-2 dissolved in 600 mL of warm benzene was added a degassed solution of 110 mL (0.79 mol) of triethylamine in 3.5 L of CH_3CN. The heat source was removed, and the reaction was protected from light with foil. A solution of 34 mL (0.46 mol) of allylamine in 500 mL of CH_3CN (degassed) was added over a period of several hours via an addition funnel, and the reaction was stirred overnight. The next day, an additional 35 mL of allylamine (0.47 mol) in 200 mL of CH_3CN was slowly added via the addition funnel.

The reaction was monitored by TLC (R_f of 3 = 0.5 eluting with 1:1 ethyl acetate hexanes). After 3 d, all but 300 mL of the solvent was removed by distillation. To the mixture was added 500 mL of CH_2Cl_2 and 500 mL of 10‰ NaOH (aqueous). The aqueous layer was extracted several times with CH_2Cl_2, and the combined CH_2Cl_2 layers were washed with brine and dried over $MgSO_4$. The solution was filtered and the solvent was removed with a rotary evaporator. The product mixture was dissolved in acetone and passed through a plug of silica gel (3-cm thick × 13-cm diameter). Most of the acetone was removed by rotary evaporation. Trituration in acetone yielded 93.5 g of 3. Another 19.8 g of 3 was isolated from the mother liquor by filtration through silica gel and trituration with acetone. The combined material (113.3 g, 88%) was sufficiently pure for the next reaction. Recrystallization from toluene gave analytically pure material: mp 148-9 °C: ^1H NMR (250 MHz, $CDCl_3$) δ 7.93–7.96 (m, 4H), 7.50–7.57 (m, 4H), 7.41–7.47 (m, 2H), 7.21–7.27 (m, 2H), 5.96–6.12 (m, 1H), 5.22–5.32 (m, 2H), 3.76 (d, *J* = 12.30 Hz, 2H), 3.18 (d, *J* = 12.35 Hz, 2H), 3.10–3.16 (m, 2H); ^{13}C NMR (53.6 MHz, $CDCl_3$) δ 136.0, 134.9, 133.2, 133.0, 131.2, 128.2, 127.6, 127.3, 125.6, 125.3, 117.9, 58.3, 54.6. Anal. Calcd for $C_{25}H_{21}N$: C, 89.51; H, 6.31; N, 4.18. Found: C, 89.53; H, 6.34; N, 4.26.

(±)-3,5-Dihydro-4*H*-dinaphth[2,1-*c*:1′,2′-*e*]azepine (1). A 2-L three-neck flask equipped with a distillation head was charged with 1.1 L of 10% aqueous ethanol and 44.0 g (0.131 mol) of (±)-3. This mixture was stirred and purged with nitrogen for 1 h. The degassing tube was removed and the solution was heated, dissolving the amine. Before reflux temperature was reached, 1.21 g (1.31 mmol, 1 mol %) of tris(triphenylphosphine)rhodium-(I) chloride was added. The reaction was driven by continuous azeotropic removal of propanal.[10] After 1 h, 800 mL of solvent had been distilled from the reaction. TLC analysis (1:1 ethyl acetate hexanes) indicated some starting material, a slightly more polar spot, and mostly 1. An additional 1 L of 10% aqueous ethanol was added and the reaction was heated 1 h. (TLC analysis indicated that 3 was consumed, but that the slightly more polar spot was still present. An aliquot of the reaction mixture was treated with 2 N HCl (aqueous) causing this side product to disappear quickly, suggesting that it was the intermediate enamine.) To the reaction mixture were added 25 mL of 20% HCl (aqueous), 200 mL of ethanol, and 100 mL of water, and most of the solvent was removed by distillation. The mixture was partitioned between ether and 10% NaOH (aqueous). The organic layer was dried over Na_2SO_4, filtered, and concentrated. Crystallization from toluene/hexanes gave 23.0 g of white crystals. The mother liquors were evaporated, and the residue was crystallized from ethyl acetate, giving 10 g of brown solid which was recrystallized twice from toluene/hexanes giving another 6.2 g of product. The combined product (75% yield) was identical to 1 made by published methods:[7] mp 149–150 °C (lit.[7] mp 147–

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149 °C); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.88–7.93 (m, 4H), 7.36–7.53 (m, 6H), 7.16–7.24 (m, 2H), 3.76 (d, J = 12.14 Hz, 2H), 3.46 (d, J = 12.13 Hz, 2H), 2.14 (s, 1H); ^{13}C NMR ($CDCl_3$, 53.6 MHz) δ 135.1, 134.7, 132.9, 131.2, 128.7, 128.1, 127.2, 126.9, 125.6, 125.2, 48.67.

3,5-Dihydro-α,β-dimethyl-4*H*-dinaphth[2,1-*c*:1′,2′-*e*]azepine-4-propanoic Acid, *tert*-Butyl Ester (mixture of isomers for reference). To 2.01 g (12.9 mmol) of *tert*-butyl tiglate was added 10.2 g (95.2) mmol) of benzylamine and the mixture was heated at reflux for 3 h. The mixture was cooled to room temperature, and most of the unreacted ester and benzylamine were removed with a kugelrohr apparatus with mild heating. Column chromatography with 20% ether in hexanes (R_f 0.5) gave 996 mg (3.78 mmol) of *tert*-butyl 3-(*N*-benzylamino)-2-methylbutanoate as a mixture of isomers (29%): IR (film) 3031, 2977, 1730, 1454, 1367, 1255, 1156, 737, 699 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$ δ 7.27–7.36 (m, 5H), 3.70–3.88 (m, 3H), 2.88–3.04 (m, 1H), 2.46–2.56 (m, 1H), 1.47 (s, 9H), 1.06–1.17 (m, 6H); ^{13}C NMR (53.6 MHz, $CDCl_3$) δ 174.79, 174.39, 140.51, 140.45, 128.10, 127.90, 126.59, 79.91, 79.73, 54.62, 54.37, 51.00, 50.96, 45.40, 44.79, 27.92, 17.45, 16.71, 12.94, 12.10.

This material was dissolved in 36 mL of methanol, treated with 1.20 g (19.0 mmol) of ammonium formate and 1 g of 10 % Pd on carbon,[24] and heated at reflux for 45 min. The reaction mixture was cooled and filtered, and the catalyst was washed with methanol and $CHCl_3$. The solvents were removed via rotary evaporation, and the residue was partitioned between $CHCl_3$ and 2% NaOH (aqueous). The aqueous layer was extracted several times with $CHCl_3$, and the combined organic extracts were washed with brine and dried over Na_2SO_4. Filtration and concentration gave 338 mg (1.95 mmol) of *tert*-butyl 3-amino-2-methylbutanoate as an oil (52%): IR (film) 2977, 2935, 1725, 1457, 1367, 1257, 1151, 853 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.81–3.00 (m, 1H), 1.97–2.14 (m, 1H), 1.28 (s, 9H), 1.15 (s, 2H), 0.89–0.95 (m, 6H); ^{13}C NMR (53.6 MHz, $CDCl_3$) δ 174.68, 174.53, 79.78, 49.16, 48.72, 48.47, 47.54, 27.76, 20.98, 20.52, 13.70, 11.86.

To a solution of 109 mg (0.630 mmol) of *tert*-butyl 3-amino-2-methylbutanoate (mixture of isomers) in 1 mL of dry benzene were added 10 mL of CH_3CN and 4 drops of triethylamine. To this solution was added 294 mg (0.668 mmol) of (±)-**2**.[9] The solution was covered with foil and heated at reflux overnight. The solvent was removed by rotary evaporation. Chromatography with 10% ether in hexanes yielded compounds at R_f 0.25 and 0.19 which were combined to give 182 mg (64%) of product as a mixture of four diastereomers: ^{1}H NMR (200 MHz, C_6D_6) δ 7.70–7.76 (m, 4H), 7.52–7.65 (m, 2H), 7.19–7.45 (m, 4H), 6.97–6.99 (m, 2H), 3.28–3.66 (m, 4H), 2.86–3.19 (m, 1H), 2.47–2.59 (m, 1H), 1.35–1.46 (m, 9H), 0.67–1.09 (m, 6H); ^{13}C NMR (53.6 MHz, C_6D_6) δ 175.31, 175.28, 174.86, 174.59, 135.44, 135.22, 135.15, 135.08, 133.49, 133.49, 133.49, 131.86, 128.92, 128.80, 128.75, 128.60, 128.39, 128.18, 126.10, 126.06, 125.59, 79.57, 79.51, 78.91, 64.23, 63.33, 63.02, 62.00, 52.90, 52.81, 52.18, 51.85, 47.11, 46.89, 46.55, 28.29, 28.20, 28.13, 16.18, 15.99, 15.26, 14.95, 14.72, 14.61, 13.66, 13.45. HPLC analysis (see general section) with 10% ether in hexanes at a flow rate of 2.00 mL/min separated the four diastereomers, retention times 34.1, 37.2, 40.0, and 45.2 min.

Adduct 4. A solution of 502 mg (1.70 mmol) of (*S*)-**1**[7] in 9 mL of DME was cooled to −63 °C before the addition of 1.06 mL of a 1.6 M solution of BuLi in hexanes (1.7 mmol). To this was added (via cannula) a −63 °C solution of 220 mg (1.55 mmol) of *tert*-butyl crotonate in 9 mL of DME. The solution was stirred at −63 °C for 1 h, 112 μL (1.80 mmol) of methyl iodide was added, and the solution was warmed to 0 °C. To this was added 10 mL of water which had been made basic with 5 drops of triethylamine, and the aqueous layer was extracted several times with ether. The combined ether extracts were rinsed with brine and dried over Na_2SO_4. Filtration, evaporation, and chromatography (first with 2:5:93 triethylamine/ether/hexanes and then with 20% ether in hexanes) yielded 494 mg (71%) of **4** (R_f of major isomer 0.29 in 20% ether). HPLC analysis (see above) showed four diastereomers in a ratio of 1:2:2:65 (shortest to longest retained): IR (film) 3054, 2974, 1726, 1457, 1367, 1354, 1207, 1156, 1139, 810 cm^{-1}; ^{1}H NMR (250 MHz, C_6D_6) δ 7.72–7.75 (m, 4H), 7.57–7.60 (m, 2H), 7.38–7.41 (m, 2H), 7.15–7.22 (m, 2H), 6.93–7.00 (m, 2H), 3.61 (d, J = 12.34 Hz, 2H), 3.51 (d, J = 12.32 Hz, 2H), 2.91 (dq, J = 10.32, 6.59 Hz, 1H), 2.50 (dq, J = 10.29, 6.81 Hz, 1H), 1.34 (s, 9H), 1.05 (d, J = 6.81 Hz, 3H), 0.73 (d, J = 6.63 Hz, 3H); ^{13}C NMR (53.6 MHz, C_6D_6) δ 174.88, 135.22, 135.17, 133.39, 131.86, 128.91, 128.74, 127.00, 126.06, 125.62, 78.91, 63.02, 52.17, 46.88, 28.18, 14.69, 13.44. Anal. Calcd for $C_{31}H_{33}NO_2$: C, 82.45; H, 7.36; N, 3.10. Found: C, 82.10; H, 7.60; N, 3.27.

(2*R*,3*R*)-*tert*-Butyl 3-(*N*-Benzoylamino)-2-methylbutanoate (5). An argon-purged three-neck flask was charged with 3.3 g of dry 20% Pd(OH)/C, 20 mL of ethanol, and 2.39 g (37.9 mmol) of ammonium formate. The mixture was heated at 50 °C for 30 min, treated with 685 mg (1.52 mmol) of adduct **4** in 25 mL of EtOH (made basic with a drop of triethylamine), and heated an additional 80 min. The reaction mixture was filtered, and the catalyst was washed with ethanol and then extracted with warm $CHCl_3$ (15 min at 50 °C). The ethanol fractions were concentrated, combined with the $CHCl_3$ extract, and partitioned with 2% NaOH (aqueous). The aqueous layer was extracted three times with $CHCl_3$ and three times with ethyl acetate. The organic extracts were dried over Na_2SO_4, filtered, and concentrated. The residue was dissolved in 5 mL of ether, cooled to 0 °C, and treated with 0.5 mL of pyridine and 176 μL (1.52 mmol) of benzoyl chloride. The reaction mixture was stirred overnight, with warming to room temperature. Water was added and the aqueous layer was extracted several times with ether. The combined ether fractions were dried over $MgSO_4$, filtered, and concentrated. Chromatography with 20% ethyl acetate in hexanes yielded 198 mg (57%) of very clean **5** (R_f 0.22) as an oil which was later crystallized from pentane: mp 92–94 °C; IR (film) 3275, 3079, 2983, 1724, 1634, 1366, 1161, 1127, 852, 700 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.77–7.82 (m, 2H), 7.39–7.47 (m, 3H), 7.38 (br d, J = 9.02 Hz, 1H), 4.31 (ddq, J = 4.12, 9.08, 6.70 Hz, 1H), 2.57 (dq, J = 4.08, 7.16 Hz, 1H), 1.45 (s, 9H), 1.24 (d, J = 6.76 Hz, 3H), 1.19 (d, J = 7.20 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.36, 166.62, 134.54, 131.21, 128.40, 126.77, 81.19, 47.48, 44.60, 27.99, 19.64, 15.27. Anal. Calcd for $C_{16}H_{23}NO_3$: C, 69.29; H, 8.35; N, 5.05. Found: C, 69.45; H, 8.53; N, 5.14.

(3*R*,4*R*)-3,4-Dimethyl-1-(phenylmethyl)azetidin-2-one (8). To a solution of 30.3 mg of **5** (0.109 mmol) in 1 mL of THF at 0 °C was added 0.22 mL of a 1.0 M BH_3·THF solution (0.22 mmol). The solution was stirred for 30 min at 0 °C and at room temperature for 1 h before being heated at reflux temperature for 30 min. Another 0.15 mL of BH_3·THF solution was added, and the solution was heated for another 1 h. The progress of the reaction was monitored by TLC, the product having an identical R_f value as *tert*-butyl 3-(*N*-benzylamino)-2-methylbutanoate (see above). The solvent was removed *in vacuo* and replaced with 3 mL of TFA. This solution was stirred for 40 min before solvent removal. The product was dissolved in 10 mL of CH_2Cl_2 to the solution were added 0.5 mL of triethylamine and 53 mg of 2-chloro-*N*-methylpyridinium iodide (0.28 mmol), and the reaction was stirred at room temperature overnight. The solution was partitioned with water, the aqueous layer was extracted several times with CH_2Cl_2, and the combined CH_2Cl_2 layers were rinsed with brine and dried over Na_2SO_4. Column chromatography was used to isolate 3.4 mg of product (R_f 0.45 in 50% ethyl acetate in hexanes, 16% yield) which had the same ^{1}H NMR as reported in the literature.[15a,b]

Adduct 6. A solution of 232 mg (0.787 mmol) of (*S*)-**1**[7] in 5 mL of DME was cooled to −63 °C before the addition of 0.49 mL of a 1.6 M BuLi solution in hexanes (0.79 mmol). After a few minutes, a solution of 102 mg (0.655 mmol) of *tert*-butyl tiglate in 5 mL of DME at −63 °C was added via cannula. The solution was stirred at −63 °C for 2 h and at −46 °C for 2 h before quenching with a solution of 49 mg of NH_4Cl and several drops of triethylamine in 10 mL of water. The aqueous layer was extracted several times with ether, and the combined ether layers were washed with brine and dried over Na_2SO_4. Chromatography (first with 2:5:93 triethylamine/ether/hexanes and then with 20% ether in hexanes) yielded 185 mg (63%) of **6** (R_f of major isomer 0.35 in 20% ether). HPLC analysis (see above) showed only three of the four possible diastereomers in a ratio of 1:24.4:0:3.8 (shortest to longest retained): IR (film) 3054, 2974, 2929, 1724, 1457, 1367, 1156, 1137, 1075, 818, 752 cm^{-1}; ^{1}H NMR of the major isomer (250 MHz, C_6D_6) δ 7.70–7.73 (m, 4H), 7.52–7.56 (m, 2H), 7.29–

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7.32 (m, 2H), 7.15–7.22 (m, 2H), 6.93–6.99 (m, 2H), 3.43 (d, J = 12.35 Hz, 2H), 3.38 (d, J = 12.38 Hz, 2H), 3.00 (dq, J = 9.87, 6.39 Hz, 1H), 2.56 (dq, J = 9.87, 6.85 Hz, 1H), 1.43 (s, 9H), 1.33 (d, J = 6.83 Hz, 3H), 1.03 (d, J = 6.47 Hz, 3H); ^{13}C NMR (53.6 MHz, C_6D_6) δ 175.25, 135.19, 135.13, 133.42, 131.88, 130.51, 128.78, 128.75, 127.82, 126.03, 125.59, 79.55, 62.00, 51.84, 46.92, 28.11, 15.95, 14.92. Anal. Calcd for $C_{31}H_{33}NO_2$: C, 82.45; H, 7.36; N, 3.10. Found: C, 82.04; H, 7.53; N, 3.04.

(2*S*,3*R*)-*tert*-Butyl-3-(*N*-Benzoylamino)-2-methylbutanoate (7). An argon-purged three-neck flask was charged with 902 mg of 20% $Pd(OH)_2/C$, 10 mL of ethanol, and 646 mg (10.3 mmol) of ammonium formate. This mixture was heated at 50 °C for 30 min and treated with 185 mg of **6** (1:24.4:0:3.8 mixture of diastereomers, 0.410 mmol) in 15 mL of ethanol made basic with one drop of triethylamine, and 100 mg of ammonium formate. After heating for 1 h, the mixture was filtered, the catalyst was washed with ethanol, and the combined filtrates were concentrated. The catalyst was stirred with 50 mL of $CHCl_3$ at 50 °C, filtered, and washed with $CHCl_3$. The $CHCl_3$ solutions were added to the residue from ethanol and partitioned with 2% NaOH (aqueous). The aqueous layer was extracted three times with $CHCl_3$ and three times with ethyl acetate. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The residue was dissolved in 5 mL of ether and cooled to 0 °C before adding 0.5 mL of pyridine and 50 μL (0.43 mmol) of benzoyl chloride. The reaction was stirred overnight with warming to room temperature. Water was added, and the mixture was extracted three times with ether and three times with ethyl acetate. The organic solvents were dried over $MgSO_4$, filtered, concentrated, and chromatographed with 20% ethyl acetate in hexanes yielding 74.9 mg of **7** (66%). The ^{1}H NMR showed a 6:1 ratio of **7** to **5**. Diasteromerically pure **7** was obtained by crystallization from hexanes: mp 113–115 °C; IR (film) 3316 (br), 3065, 2978, 1727, 1637, 1540, 1491, 1368, 1278, 1159, 851, 712, 695 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73–7.77 (m, 2H), 7.39–7.46 (m, 3H), 7.00 (br d, J = 8.60 Hz, 1H), 4.32 (ddq, J = 4.67, 8.93, 6.72 Hz, 1H), 2.64 (dq, J = 4.70, 7.17 Hz, 1H), 1.45 (s, 9H), 1.19 (d, J = 6.73 Hz, 3H), 1.16 (d, J = 7.20 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.47, 166.20, 134.64, 131.24, 128.41, 126.73, 81.18, 47.54, 44.72, 28.05, 16.42, 13.97. Anal. Calcd for $C_{16}H_{23}NO_3$: C, 69.29; H, 8.35; N, 5.05. Found: C, 69.11; H, 8.54; N, 5.04.

(3*S*,4*R*)-3,4-Dimethyl-1-(phenylmethyl)azetidin-2-one (9). This β-lactam was made in the same manner as lactam **8**; 38.1 mg of diasteromerically pure **7** was converted into 2.5 mg of **9** (10% yield): $[\alpha]_D$ = +27.6° (c = 0.25, $CHCl_3$) indicates that the product is the 3*S*,4*R* isomer (lit.[15b] $[\alpha]_D$ of 3*R*,4*S* isomer is −29.2° (c = 0.69, $CHCl_3$).

Acknowledgment. J.M.H. thanks the National Science Foundation (Presidential Young Investigator Award, CHE-8857453), the Camille and Henry Dreyfus Foundation (Teacher-Scholar Award), the Shell Oil Co. Foundation (Shell Faculty Fellowship), the Merck Sharp & Dohme Research Laboratories, the Xerox Corp., the Monsanto Co., Hoffmann-La Roche Inc., and Eli Lilly and Co. for financial support.