Synthesis of *N*-Boc-*β*-Aryl Alanines and of *N*-Boc-*β*-Methyl-*β*-aryl Alanines by Regioselective Ring-Opening of Enantiomerically Pure *N*-Boc-Aziridines

Eva Medina, Albert Moyano, Miquel A. Pericàs,*,† and Antoni Riera*,‡

Unitat de Recerca en Síntesi Asimètrica (URSA), Departament de Química Orgànica, Universitat de Barcelona, c/ Martí i Franquès, 1-11. 08028-Barcelona, Spain

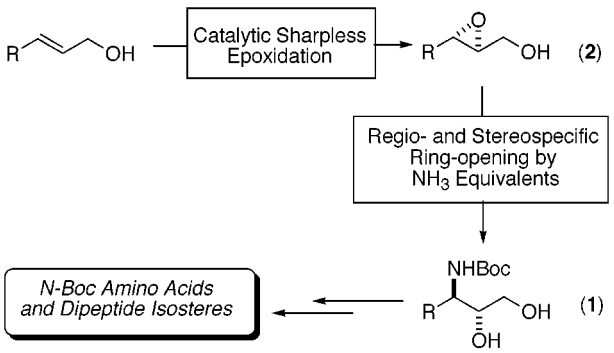
Received June 15, 1998

Introduction

The stereoselective synthesis of unnatural α-amino acids[1] is currently a subject of enormous interest mainly due to the increasing biological and therapeutic applications of modified peptides.[2] Over the last few years, we have been involved in a project devoted to the enantioselective synthesis of several structural types of *N*-Boc amino acids and dipeptide isosteres.[3,4] Our approach, which is based on the intermediacy of enantiomerically pure *N*-Boc-3-amino-1,2-diols **1**, readily available from allyl alcohols through Sharpless epoxidation[5] followed by a regio- and stereospecific ring-opening by a convenient ammonia equivalent[6] (Scheme 1), has even found application at the industrial level.[7]

As an application of this methodology, we have recently reported a more convenient synthesis of *N*-Boc arylglycines **3**.[8] In that particular case, our approach benefits from several aspects that make it attractive in front of possible alternatives: (a) the easy availability of aromatic carbaldehydes which are the precursors of the allyl alcohols used in the Sharpless epoxidation, (b) the benzylic nature of the C-3 carbon in the epoxides **2** (R = aryl), which efficiently controls the regioselectivity of the ring opening process, and (c) the crystalline nature of the *N*-Boc-3-amino-1,2-diols **1** (R = aryl) which allows, if necessary, an easy enantioenrichment.

Scheme 1



However, if the procedure described in Scheme 1 had to be applied to the synthesis of the even more interesting *β*-aryl alanines **4**,[9,10] these advantages would be at least partially lost. In particular, the strict regiocontrol in the epoxide ring-opening derived from the benzylic nature of the attacked carbon atom would be no longer operating. To circumvent this difficulty, we planned to accede the *β*-aryl alanines from *N*-Boc-3-aryl-3-amino-1,2-propanediols (**1** R= aryl), but introduce in the sequence a 1,2-nitrogen shift instead of the degradative oxidation step. This would be done through the intermediacy of *N*-Boc aziridines **5** (Scheme 2), which present a benzyl type carbon for nucleophilic attack and offer the additional bonus of easily allowing the preparation of *β*-substituted derivatives **6**.

We report here a new and simple procedure for the preparation of optically pure *β*-aryl alanines (**4**) and *β*-alkyl-*β*-aryl alanines (**6**), from readily available *N*-Boc-3-aryl-3-amino-1,2-propanediols (**1**, R = aryl).

Results and Discussion

Phenyl and 1-naphthyl were selected as representative aryl groups for our study. In both cases, the preparation

† E-mail: mpb@ursa.qo.ub.es.
‡ E-mail: are@ursa.qo.ub.es.

(1) (a) Duthaler, R. O. *Tetrahedron* **1994**, *50*, 1539−1650. (b) Ohfune, Y. *Acc. Chem. Res.* **1992**, *25*, 360−366 (c) Williams, R. M. *Synthesis of Optically Active* α*-Amino Acids*; Pergamon Press: Oxford, 1989. (d) O'Donnell, M. J., Ed. *Tetrahedron* **1988**, *44*, 5253−5614.

(2) (a) Begley, D. J. *J. Pharm. Pharmacol.* **1996**, *48*, 136−146. (b) McMartin, C. *Handb. Exp. Pharmacol.* **1994**, *110*, 371−382 (c) Crommelin, D. J. A.; Storm, G. *Eur. J. Pharm. Sci.* **1994**, *2*, 17−18. (d) Kompella, U. B.; Lee, V. H. L. *Adv. Drug Delivery Rev.* **1992**, *8 (1)*, 115−162.

(3) (a) Poch, M.; Alcón, M.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron Lett.* **1993**, *34*, 7781−7784. (b) Pastó, M.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron: Asymmetry* **1995**, *6*, 2329−2342. (c) Castejón, P.; Pastó, M.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron Lett.* **1995**, *36*, 3019−3022. (d) Castejón, P.; Moyano, A.; Pericàs, M. A.; Riera, A. *Chem. Eur. J.* **1996**, *2*, 1001−1006. (e) Castejón, P.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron* **1996**, *52*, 7063−7086. (f) Pastó, M.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron: Asymmetry* **1996**, *7*, 243−262. (g) Pastó, M.; Castejón, P.; Moyano, A.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **1996**, *61*, 6033−6037. (h) Pastó, M.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron Lett.* **1998**, *39*, 1233−1236. (i) Aguilar, N.; Moyano, A.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **1998**, *63*, 3560−3567.

(4) Pastó, M.; Moyano, A.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **1997**, *62*, 8425−8431.

(5) (a) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765−5780. (b) Katsuki, T.; Martín, V. S. *Org. React.* **1996**, *48*, 1−299.

(6) Canas, M.; Poch, M.; Verdaguer, X.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron Lett.* **1991**, *32*, 6931−6934.

(7) Shum, W. P.; Cannarsa, M. J. In *Chirality in Industry II*; Collins, A. N., Sheldrake, G. N., Crosby, J., Eds.; John Wiley & Sons Ltd.: New York, 1997; pp 363−379.

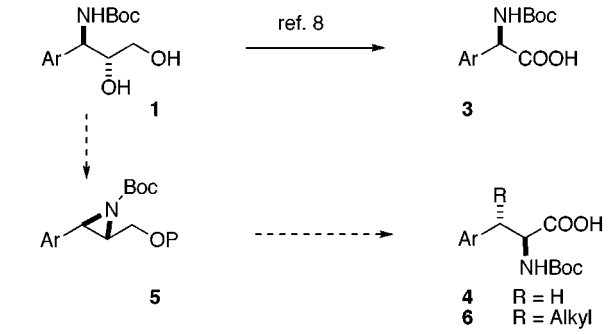
(8) Medina, E.; Vidal-Ferran, A.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron: Asymmetry* **1997**, *8*, 1581−1586.

(9) Selected examples of modified peptides wiith naphthyl alanines: (a) Rodriguez, M.; Bernad, N.; Galas, M. C.; Lignon, M. F.; Laur, J.; Aumelas, A.; Martinez, J. *Eur. J. Med. Chem.* **1991**, *26*, 245−253. (b) Prochazka, Z.; Slaninova, J. *Collect. Czech. Chem. Commun.* **1995**, *60*, 2170−2177. (c) Ranjalahy-Rasoloarijao, L.; Lazaro, R.; Daumas, P.; Heitz, F. *Int. J. Pept. Protein Res.* **1989**, *33*, 273−280. (d) Lammek, B.; Konieczna, E.; Trzeciak, H. I.; Kozlowski, A.; Szymkowiak, J.; Stojko, R.; Kupryszewski, G. *J. Pharm. Pharmacol.* **1996**, *48*, 316−319. (e) Lammek, B.; Czaja, M.; Derdowska, I.; Rekowski, P.; Trzeciak, H. I.; Sikora, P.; Szkrobka, W.; Stojko, R.; Kupryszewski, G. *J. Pept. Res.* **1997**, *49*, 261−268. (f) Mierke, D. F.; Said-Nejad, O. E.; Schiller, P. W.; Goodman, M. *Biopolymers* **1990**, *29*, 179−196. (g) Schmidt, R.; Wilkes, B. C.; Chung, N. N.; Lemieux, C.; Schiller, P. W. *Int. J. Pept. Protein Res.* **1996**, *48*, 411−419. (h) Yabe, Y.; Miura, C.; Baba, Y.; Sawano, S. *Chem. Pharm. Bull.* **1978**, *26*, 993−997.

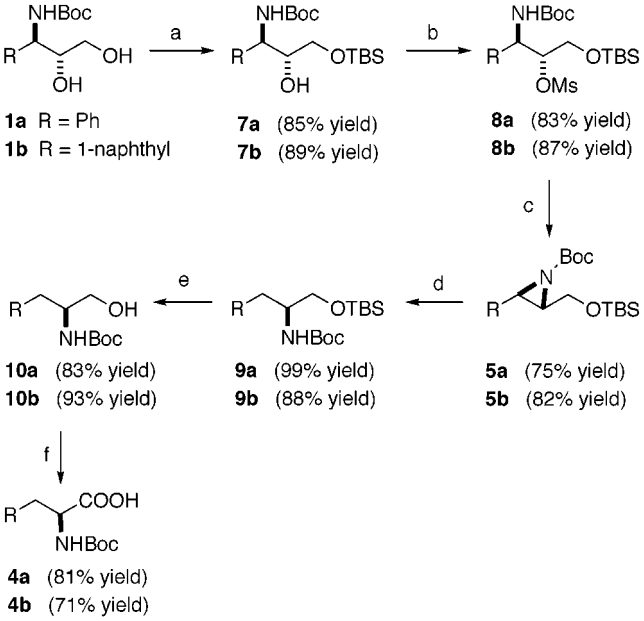
(10) Some references of asymmetric synthesis of *β*-aryl alanines: (a) Chan, A. S. C.; Hu, W.; Pai, C.-C.; Lau, C.-P.; Jiang, Y.; Mi, A.; Yan, M.; Sun, J.; Lou, R.; Deng, J. *J. Am. Chem. Soc.* **1997**, *119*, 9570−9571. (b) Zhu, G.; Cao, P.; Jiang, Q.; Zhang, X. *J. Am. Chem. Soc.* **1997**, *119*, 1799−1800. (c) Kolar, P.; Petric, A.; Tisler, M. *J. Heterocycl. Chem.* **1997**, *34*, 1067−1098. (d) Meiwes, J.; Schudok, M.; Kretzschmar, G. *Tetrahedron: Asymmetry* **1997**, *8*, 527−536. (e) Tararov, V. I.; Saveleva, T. F.; Kuznetsov, N. Y.; Ikonnikov, N. S.; Orlova, S. A.; Belokon, Y. N.; North, M. *Tetrahedron: Asymmetry* **1997**, *8*, 79−83. (f) Jackson, R. F. W.; Wythes, M. J.; Wood, A. *Tetrahedron Lett.* **1989**, *30*, 5941−5944.

10.1021/jo981140i CCC: $15.00
Published on Web 10/28/1998

Scheme 2



Scheme 3[a]



[a] Reagents and conditions: (a) Bu^{t}Me$_2$SiCl, imidazole, DMF, rt; (b) CH_3SO_2Cl, Et_3N, 4-DMAP, CH_2Cl_2; (c) HNa, THF; (d) H_2, Pd/C, AcEt; (e) TBAF, THF; (f) PDC, DMF.

of the corresponding enantiomerically pure *N*-Boc-3-amino-1,2-diols[3a,3f,8] is well documented and can be very easily performed. Starting from these aminodiols (**1a,b**), the primary alcohol was first protected (Scheme 3) as a *tert*-butyldimethylsilyl ether under standard conditions to afford **7a,b** with excellent yield (85−89%) and complete chemoselectivity. The conversion of these ethers into the derived *N*-Boc aziridines **5a,b** was then attempted using Mitsunobu conditions (DEAD, PPh_3),[11] but probably due to the low nucleophilicity of the carbamate nitrogen atom, the cyclization yields were rather low (20−34%). Quite gratifyingly, this cyclization could be conveniently performed by mesylation of the secondary alcohol, leading to **8a,b**, and subsequent generation of the anion of the carbamate with sodium hydride. In this way, *N*-Boc-aziridines **5a,b** were obtained in 62−71% yield.

With the key aziridines **5** in hand, reductive conversion to β-aryl alanine precursors was first studied by catalytic hydrogenation. To our satisfaction, the reaction took place in excellent yield and with complete regioselectivity, affording the protected amino alcohols **9a,b**. Then, a selective deprotection of the silyl ether (TBAF/THF) and subsequent oxidation of the primary alcohol in **10a,b** with PDC in DMF afforded the target β-aryl alanines **4a,b** in 58−67% overall yield from aziridines **5a,b** (Scheme 3).

To check the enantiomeric purity of these amino acids, the corresponding methyl esters, prepared by treatment with methyl iodide and potassium hydrogen carbonate in DMF, were analyzed by HPLC (Chiracel OD). In both cases the enantiomeric purity was very high (>99% ee for **4a** and >98% ee for **4b**), in full agreement with the optical purity of the starting *N*-Boc-3-amino-1,2-diols **1**.

As we have already mentioned, the ring opening of *N*-Boc-aziridines **5** by carbon nucleophiles could lead to β-substituted β-aryl alanines which are important bioactive compounds. In particular, several β-methyl-β-aryl alanines have been incorporated into peptides in order to confer conformational restrictions to the molecule[12] and modify their biological activities.[13] The demand for flexible stereoselective methods allowing the preparation of any desired diastereomer of such amino acids has only recently met a satisfactory answer[4] in the case of β-methyl-phenylalanine.[14] In this context, the planned ring opening of the *N*-Boc-aziridines with carbon nucleophiles could be the key step of a new and practical synthesis of such amino acids with anti configuration.

Although the protection of the aziridine nitrogen with a *tert*-butoxycarbonyl group is well-known,[15] the activation of the aziridine ring by this group has received very little attention.[16] Notwithstanding, the reaction of **5a,b** with lithium dimethylcuprate took place cleanly to afford with regioselectivity and with excellent yields the protected 2-amino-3-arylbutanols **11a,b** (Scheme 4). The conversion of these intermediates into the target amino acids **6a,b** was easily performed by a sequence of fluoride-induced deprotection (75−93% yield) and oxidation of the intermediate alcohols **12a,b** with PDC in DMF (77−83%), as for the β-unsubstituted analogues.

The so-prepared *anti*-*N*-Boc-β-methylphenylalanine **6a** was spectroscopically identical to the one previously obtained by us,[4] and its optical purity was determined to be greater than 99% ee by HPLC analysis of its methyl ester. On the other hand, the previously unreported *anti*-*N*-Boc-β-methyl-β-naphthyl alanine **6b** was completely characterized, and its optical purity was also checked by HPLC (>97% ee). This new compound has a great potential interest for structural and biological studies, since it combines two of the most usual modifications of phenylalanine used in peptides: replacement of the phenyl group for a naphthyl and alkyl substitution at the β-position.[17]

(11) Osborn, H. M. I.; Sweeney, J. *Tetrahedron: Asymmetry* **1997**, *8*, 1693−1715.

(12) (a) Burgess, A. W. *Proc. Natl. Acad. Sci. U.S.A.* **1994**, *91*, 2649−2653. (b) Hruby, V. J. *Biopolymers* **1993** *33*, 1073−1082. (c) Hruby, V. J.; Al-Obeidi, F.; Kazmierski, W. *Biochem. J.* **1990**, *268*, 249−262. (d) Shenderovich, M. D.; Kövér, K. E.; Nikiforovich, G. V.; Jiao, D.; Hruby, V. J. *Biopolymers* **1996**, *38*, 141−56.

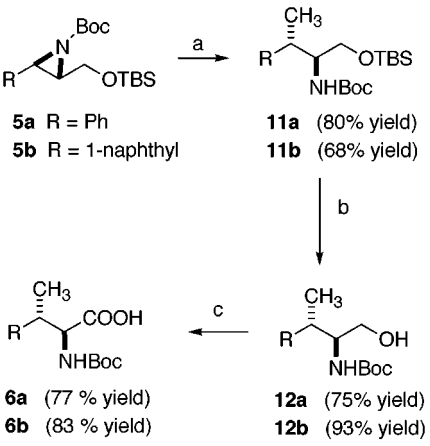
(13) (a) Hruby, V. J.; Toth, G.; Gherig, C. A.; Kao, L.-F.; Knapp, R.; Lui, G. K.; Yamamura, H. I.; Kramer, T. H.; Davis, P.; Burks, T. F. *J. Med. Chem.* **1991**, *34*, 1823−1830. (b) Qian, X.; Shenderovich, M. D.; Kövér, K. E.; Davis, P.; Horváth, R.; Zalewska, T.; Yamamura, H. I.; Porreca, F.; Hruby, V. J. *J. Am. Chem. Soc.* **1996**, *118*, 7280−7290.

(14) (a) Dharanipragada, R.; Nicolas, E.; Toth, G.; Hruby, V. J. *Tetrahedron Lett.* **1989**, *30*, 6841−6844. (b) Dharanipragada, R.; VanHulle, K.; Bannister, A.; Bear, S.; Kennedy, L.; Hruby, V. J. *Tetrahedron* **1992**, *48*, 4733−4748. (c) Burk, M. J.; Gross, M. F.; Martinez, J. P. *J. Am. Chem. Soc.* **1995**, *117*, 9375−9376. (d) Davis, F. A.; Liang, C.-H.; Liu, H. *J. Org. Chem.* **1997**, *62*, 3796−3797.

(15) (a) Wessig, P.; Schwarz, J. *Synlett* **1997**, 893−894 (b) McCort, I.; Duréault, A.; Depezay, J.-C. *Tetrahedron Lett.* **1996**, *37*, 7717−7720. (c) Ziegler, F. E.; Belema, M. *J. Org. Chem.* **1994**, *59*, 7962−7967.

(16) (a) Righi, G.; Franchini, T.; Bonini, C. *Tetrahedron Lett.* **1998**, *39*, 2385−2388. (b) Ezquerra, J.; Pedregal, C.; Lamas, C.; Pastor, A.; Alvarez, P.; Vaquero, J. J. *Tetrahedron Lett.* **1996**, *37*, 683−686.

Scheme 4[a]



[a] Reagents and conditions: (a) Me_2CuLi, THF; (b) TBAF, THF; (c) PDC, DMF.

In summary, we have developed a new procedure for the synthesis of enantiomerically pure β-aryl alanines and β-alkyl substituted β-aryl alanines. Our methodology takes advantage of the convenient preparation of optically pure *N*-Boc-3-aryl-3-amino-1,2-diols using the Sharpless epoxidation as a source of chirality and is based on the conversion of these compounds into optically active *N*-Boc-aryl aziridines, which can be regioselectively hydrogenated or opened by a organocuprate. Extension of this methodology to the stereocontrolled preparation of other β-substituted alanines is underway in our laboratories and will be reported in due term.

Experimental Section

General Methods. Optical rotations were measured at room temperature (23 °C) (concentration in g/100 mL). Melting points were determined in open capillary tubes and are uncorrected. Infrared spectra were recorded using NaCl film or KBr pellet techniques. ^{1}H NMR were recorded at 200 MHz (s = singlet, d = doublet, t = triplet, q = quartet, dt = double triplet, m = multiplet, b = broad, and bd = broad doublet). ^{13}C NMR were recorded at 50.3 or 75.4 MHz. Carbon multiplicities have been assigned by distortionless enhancement by polarization transfer (DEPT) experiments. High-resolution mass spectra (CI) were performed by the Servicio de Espectrometría de Masas, Universidad de Córdoba. Elemental analyses were performed by the Servei d'Anàlisis Elementals del CSIC de Barcelona. Chromatographic separations were carried out using NEt_3-pretreated (2.5% v/v) SiO_2 (70−230 mesh). Chromatographic analyses were performed on a instrument equipped with a Chiralcel OD (25 cm) column. THF and diethyl ether were distilled over metallic sodium/benzophenone. DMF and methylene chloride were distilled over calcium hydride.

(2*R*,3*R*)-3-(*tert*-Butoxycarbonylamino)-3-phenyl-1,2-propanediol **1a**[3f] and (2*R*,3*R*)-3-(*tert*-butoxycarbonylamino)-3-(1-naphthyl)-1,2-propanediol **1b**[8] were prepared according to described procedures.

(2*R*,3*R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-[(*tert*-butoxycarbonyl)amino]-3-phenyl-2-propanol, 7a. To a solution of (2*R*,3*R*)-3-[(*tert*-butoxycarbonyl)amino]-3-phenyl-1,2-propanediol **1a** (300 mg, 1.12 mmol) in dimethylformamide (5 mL) were added *tert*-butyldimethylsilyl chloride (186 mg, 1.23 mmol) and imidazole (168 mg, 2.47 mmol). The reaction was monitored by TLC. After 24 h, water (8 mL) was added, and the aqueous phase was extracted with diethyl ether (3 × 6 mL). The combined organic phases were washed with saturated NH_4Cl aqueous solution and dried over $MgSO_4$, and the solvents were evaporated in vacuo. The crude product was purified by chromatography (AcOEt/hexane 0−5%) yielding 365 mg of **7a** as a white solid (85% yield). $[\alpha]_D = -25.9$ (*c* 2.1, $CHCl_3$). Mp: 43−45 °C. IR (film) ν_{max}: 3410, 2960, 1700, 1500 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.06 (s, 3H), 0.93 (s, 9H), 1.41 (s, 9H), 2.7 (broad s, 1H, OH), 3.4 (dd, J = 10.4 Hz, J = 4.2 Hz, 1H), 3.6 (dd, J = 10.4 Hz, J = 3.8 Hz, 1H), 3.8 (m, 1H), 4.9 (m, 1H), 6.1 (broad d 1H, NH), 7.3 (s, 5H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ −5.6 (CH_3) 18.0 (C), 25.8 (CH_3), 28.3 (CH_3), 58 (CH), 63.9 (CH_2), 72.8 (CH), 79.3 (C), 126.8 (CH), 127.3 (CH), 128.4 (CH), 139.3 (C), 155.5 (C) ppm. Anal. Calcd for $C_{20}H_{35}NO_4Si$: C, 62.95%; H, 9.25%; N, 3.67%. Found: C, 63.14%; H, 9.23%; N, 3.62%.

(2*R*,3*R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-[(*tert*-butoxycarbonyl)amino]-3-(1-naphthyl)-2-propanol, 7b. The procedure described in the preparation of **7a** but starting from 0.93 g (2.93 mmol) of **1b** afforded 1.13 g of **7b** as a white solid (89% yield). $[\alpha]_D = +15.0$ (*c* 1.0, $CHCl_3$). Mp: 71−72 °C. IR (KBr) ν_{max}: 3401, 2931, 1692, 1506 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.14 (s, 6H), 1.03 (s, 9H), 1.34 (s, 9H), 2.89 (d J = 8.8 Hz, 1H, OH), 3.59 (dd, J = 10.6 Hz, J = 3.2 Hz, 1H), 3.66 (dd, J = 10.6 Hz, J = 3.0 Hz, 1H), 4.1 (broad s, 1H), 5.9 (broad s, 1H), 6.5 (broad d, 1H), 7.5−8.25 (m, 7H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ −5.7 (CH_3) 18.2 (C), 25.8 (CH_3), 28.3 (CH_3), 55.3 (CH), 63.9 (CH_2), 71.2 (CH), 79.3 (C), 122.8 (CH), 123.2 (CH), 125.2 (CH), 125.6 (CH), 126.3 (CH), 128.0 (CH), 128.8 (CH), 130.5 (C), 134.3 (C), 136.3 (C), 155.3 (C) ppm. EM (CI−NH_3) m/e = 432 (M^+ + 1, 51), 376 (100), 332 (23). Anal. Calcd for $C_{24}H_{37}NO_4Si$: C, 66.78%; H, 8.64%; N, 3.24%. Found: C, 66.82%; H, 8.78%; N, 3.37%.

Methanesulfonic Acid (1*R*,2*R*)-2-[(*tert*-Butoxycarbonyl)amino]-1-[[(*tert*-butyldimethylsilyl)oxy]methyl]-2-phenylethyl Ester, 8a. To a solution of **7a** (1.86 g, 4.88 mmol) in CH_2Cl_2 (5 mL) at −15 °C were added triethylamine (0.75 mL, 5.37 mmol), 4-(*N*,*N*-dimethylamino)pyridine (30 mg, 0.24 mmol), and methanesulfonyl chloride (0.41 mL, 5.37 mmol). The mixture was allowed to warm to room temperature under stirring, and the reaction progress was monitored by TLC. When no starting material could be detected (ca. 5 h), water (10 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic phases were washed with cold 10% aq HCl, $NaHCO_3$ satd solution and water, dried over $MgSO_4$, concentrated in vacuo, and purified by column chromatography (AcOEt/hexanes 10−15%) to afford 1.87 g (83% yield) of **8a** as an oil. $[\alpha]_D = -9.6$ (*c* 2.0, $CHCl_3$). IR (KBr) ν_{max}: 3400, 2960, 1710, 1500 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.05 (s, 3H), 0.08 (s, 3H), 0.93 (s, 9H), 1.42 (s, 9H), 3.00 (s, 3H), 3.62 (dd, J = 12 Hz, J = 4.1 Hz, 1H), 3.74 (dd, J = 12 Hz, J = 3.7 Hz, 1H,), 4.87 (m, 1H), 5.10 (broad s, 1H), 6.15 (broad d, 1H, NH), 7.34 (s, 5H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ −5.7 (CH_3) 18.0 (C), 25.7(CH_3), 28.2 (CH_3), 38.6 (CH_3), 56.2 (CH), 62.9 (CH_2), 79.4 (C), 82.0 (CH), 127.2 (CH), 128.6 (CH), 128.0 (CH), 137.4 (C), 155.1 (C) ppm. EM (CI−NH_3) m/e = 477 (M^+ + 18, 100), 460 (M^+ + 1, 15), 421 (18).

Methanesulfonic Acid (1*R*,2*R*)-2-[(*tert*-butoxycarbonyl)amino]-1-[[(*tert*-butyldimethylsilyl)oxy]methyl]-2-(1-naphthyl)ethyl Ester, 8b. The procedure described in the preparation of **8a** but starting with 1.0 g (2.31 mmol) of **7b** afforded 1.02 g of **8b** as a colorless oil (87% yield). $[\alpha]_D = +38.3$ (*c* 1.0, $CHCl_3$). IR (KBr) ν_{max}: 3411, 2932, 1717, 1503 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.03 (s, 6H), 0.92 (s, 9H), 1.38 (s, 9H), 3.03 (s, 3H), 3.55 (dd, J = 12 Hz, 1H), 3.70 (dd, J = 12 Hz, J = 2.4 Hz, 1H), 5.01 (s, 1H), 6.09 (dd, J = 7.6, J = 4.8 Hz, 1H), 6.65 (broad d 1H, NH), 7.4−8.2 (m, 7H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ −5.8 (CH_3), 18.0 (C), 25.6 (CH_3), 28.1 (CH_3), 38.7 (CH_3), 53.0 (CH), 63.0 (CH_2), 79.3 (C), 79.3 (CH), 122.4 (CH), 123.9 (CH), 125.1 (CH), 125.7 (CH), 126.7 (CH), 128.5 (CH), 128.7 (CH), 130.6 (C), 134.1 (C), 134.2 (C), 155.6 (C) ppm. EM (CI−NH_3) m/e = 510 (M^+ + 1, 50), 454 (100), 410 (21).

(2*S*,3*R*)-1-(*tert*-Butoxycarbonyl)-2-[[(*tert*-butyldimethylsilyl)oxy]methyl]-3-phenylaziridine, 5a. To a suspension of sodium hydride (13.05 mmol, from 392 mg of a 80% mixture with paraffin washed with anhydrous hexane under nitrogen) in THF (7 mL) was added a solution of **8a** (1.5 g, 3.26 mmol) in THF (10 mL). After 3 h of stirring at room temperature, ethyl acetate (5 mL) and some drops of methanol were added to the mixture to

(17) The synthesis of four isomers of β-methyl-3-(2-naphthyl)alanine has been reported recently: Yuan, W.; Hruby, V. J. *Tetrahedron Lett.* **1997**, *38*, 3853−3856.

remove any trace of unreacted hydride. The solvent was removed at reduced pressure, and the crude mixture was treated with a 1:1 mixture of H_2O/AcOEt. The aqueous phase was extracted with ethyl acetate (3 × 7 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated. Purification of the crude mixture by column chromatography (AcOEt/hexanes 3%) gave 0.89 g of aziridine **5a** as a colorless oil (75% yield). $[\alpha]_D = -54.6$ (*c* 1.1, EtOH). IR (film) ν_{max}: 2931, 1721 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 0.09 (s, 3H), 0.11 (s, 3H), 0.92 (s, 9H), 1.39 (s, 9H), 2.8 (m, 1H), 3.5 (d, $J = 3.4$ Hz, 1H), 3.92 (dd, $J = 11.5$ Hz, $J = 3.7$ Hz, 1H), 4.05 (dd, $J = 10.4$ Hz, $J = 11.5$ Hz, $J = 3.2$ Hz, 1H), 7.3 (s, 5H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ −5.2 (CH_3), 18.4 (C), 25.9 (CH_3), 28.0 (CH_3), 41.5 (CH), 46.6 (CH), 60.3 (CH_2), 81.0 (C), 126.7 (CH), 127.6 (CH), 128.3 (CH), 136.6 (C), 160.7 (C) ppm. EM (CI−NH_3) *m/e* = 381 (M^+ + 18, 5), 364 (M^+ + 1, 60), 325 (100). HRMS (CI) calcd for $C_{20}H_{34}O_3NSi$: 364.2308. Found: 364.2317.

(2*S*,3*R*)-1-(*tert*-Butoxycarbonyl)-2-[[(*tert*-butyldimethylsilyl)oxy]methyl]-3-(1-naphthyl)-aziridine, 5b. The procedure described in the preparation of **5a** but starting with 460 mg of **8b** afforded 309 mg of aziridine **5b** as a white solid (82% yield). $[\alpha]_D = -67.2$ (*c* 0.97, $CHCl_3$). Mp: 63−65 °C. IR (KBr) ν_{max}: 2933, 1719 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 0.15 (s, 6H), 0.96 (s, 9H), 1.37 (s, 9H), 2.84 (m, 1H), 3.92 (dd, $J = 11.4$ Hz, $J = 4.6$ Hz, 1H), 4.05 (d, $J = 3.4$ Hz), 4.27 (dd, $J = 11.4$ Hz, $J = 3.4$ Hz, 1H), 7.4−8.4 (m, 7H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ −5.3 (CH_3) 18.6 (C), 25.9 (CH_3), 27.9 (CH_3), 40.6 (CH), 45.2 (CH), 60.9 (CH_2), 81.0 (C), 123.9 (CH), 124.2 (CH), 125.4 (CH), 125.8 (CH), 126.1 (CH), 128.1 (CH), 128.4 (CH), 132.1 (C), 132.7 (C), 133.3 (C), 159.7 (C) ppm. EM (CI−NH_3) *m/e* = 431 (M^+ + 18, 100), 414 (M^+ + 1, 68), 375 (100), 376 (29). Anal. Calcd for $C_{24}H_{35}NO_3Si$: C, 69.69%; H, 8.52%; N, 3.38%. Found: C, 69.71%; H, 8.60%; N, 3.32%.

(2*S*)-2-[(*tert*-Butoxycarbonyl)amino]-1-[(*tert*-Butyldimethylsilyl)oxy]-3-phenylpropane, 9a. A solution of aziridine **5a** (205 mg, 0.56 mmol) in ethyl acetate (3 mL) was added to a stirred suspension of 10% Pd/C (30 mg) in ethyl acetate (1.2 mL) under hydrogen. The mixture was hydrogenated at atmospheric pressure (hydrogen balloon) until no starting material could be detected by TLC (ca. 4 h). Then, the suspension was filtered through Celite, washing the filtrate thoroughly with AcOEt and MeOH. The solvents were evaporated at reduced pressure yielding 206 mg of a crude product that was spectroscopically pure (quantitative yield). $[\alpha]_D = -22.8$ (*c* 1.1, $CHCl_3$). IR (film) ν_{max}: 3452, 2930, 1719, 1497, 1254, 1171, 837 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.92 (s, 9H), 1.42 (s, 9H), 2.8 (d, $J = 7$ Hz, 2H), 3.45−3.57 (m, 2H), 3.82 (s, 1H), 4.73 (broad s, 1H, NH), 7.2−7.35 (m, 5H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ −5.2 (CH_3), 18.4 (C), 25.9 (CH_3), 28.3 (CH_3), 37.3 (CH_2), 53.0 (CH), 62.8 (CH_2), 81.0 (C), 126.2 (CH), 128.3 (CH), 129.4 (CH), 139.9 (C), 154.0 (C) ppm. EM (CI−NH_3) *m/e* = 383 (M^+ + 18, 9), 366 (M^+ + 1, 100). HRMS (CI) calcd for $C_{16}H_{30}NOSi$ (M^+ − Boc): 280.2097. Found: 280.2089.

(2*S*)-2-[(*tert*-butoxycarbonyl)amino]-1-[(*tert*-Butyldimethylsilyl)oxy]-3-(1-naphthyl)propane, 9b. The procedure described in the preparation of **9a** but starting with **5b** (76 mg, 0.18 mmol) afforded after chromatographic purification (AcOEt/hexanes 0−2%) 68 mg of **9b** (88% yield). $[\alpha]_D = -35.0$ (*c* 0.8, $CHCl_3$). IR (KBr) ν_{max}: 3450, 2931, 1713, 1491 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 0.05 (s, 3H), 0.06 (s, 3H,), 0.96 (s, 9H), 1.44 (s, 9H), 3.15−3.5 (m, 4H), 4.01 (s, broad, 1H), 4.95 (broad d, 1H), 7.3−8.4 (m, 7H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ −5.4 (CH_3) 18.4 (C), 25.9 (CH_3), 28.4 (CH_3), 34.4 (CH_2), 52.2 (CH), 62.6 (CH_2), 78.9 (C), 124.2 (CH), 125.3 (CH), 125.5 (CH), 126.1 (CH), 127.1 (CH), 127.7 (CH), 128.6 (CH), 132.3 (C), 133.7 (C), 134.5 (C), 155.5 (C) ppm. EM (CI−CH_4): *m/e* = 416 (M^+ + 1, 92), 360 (100), 316 (33).

(2*S*)-2-[(*tert*-Butoxycarbonyl)amino]-3-phenyl-1-propanol, 10a. To a solution of **9a** (120 mg, 0.33 mmol) in THF (1.7 mL) at 0 °C was added a solution of tetrabutylammonium fluoride monohydrate (0.17 g, 0.65 mmol) in THF (1 mL). The reaction was stirred at room temperature and monitored by TLC. After 60 min, the solution was washed with water and the organic layer extracted with ether. The combined organic phases were dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by chromatography (AcOEt/hexane), yielding 68 mg (83% yield) of **10a** as a white solid. $[\alpha]_D = -25.0$ (*c* 1.0, $CHCl_3$). Mp:73−75 °C. IR (film) ν_{max}: 3357, 1686, 1528 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ: 1.4 (s, 9H), 2.35 (s, broad, 1H, OH), 2.84 (d, $J = 6.8$ Hz, 2H), 3.52−3.69 (m, 2H), 3.87 (m, 1H), 4.75 (broad d, $J = 8.4$ Hz, 1H, NH), 7.2−7.35 (m, 5H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ 28.3 (CH_3), 37.4 (CH_2), 53.7 (CH), 64.3 (CH_2), 79.7 (C), 126.5 (CH), 128.5 (CH), 129.3 (CH), 137.8 (C), 156.5 (C) ppm. EM (CI−NH_3) *m/e* = 286 (M^+ + 35, 4), 269 (M^+ + 18, 100), 252 (M^+ + 1, 83). Anal. Calcd for $C_{14}H_{21}NO_3$: C, 66.91%, H, 8.42%; N, 5.57%. Found: C, 66.86%; H, 8.51%; N, 5.52%.

(2*S*)-2-[(*tert*-Butoxycarbonyl)amino]-3-(1-naphthyl)-1-propanol, 10b. Following the procedure described in the preparation of **10a** but starting with 68 mg (0.16 mmols) of **9b**, 46 mg of **10b** was obtained as a white solid (93% yield). $[\alpha]_D = -55.7$ (*c* 1.0, $CHCl_3$). Mp: 122−123 °C. IR (KBr) ν_{max}: 3367, 2975, 1684, 1532 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 1.4 (s, 9H), 3.1 (broad s, 1H, OH), 3.3 (m, 2H), 3.58 (dd, $J = 11$ Hz, $J = 4.8$ Hz, 1H), 3.67 (dd, $J = 11$ Hz, $J = 4.8$ Hz, 1H), 4−4.09 (m, 1H), 4.9 (broad s, 1H), 7.3−8.2 (m, 7H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ 28.3 (CH_3), 34.5 (CH_2), 53.1 (CH), 64.1 (CH_2), 79.5 (C), 123.8 (CH), 125.4 (CH), 125.6 (CH), 126.2 (CH), 127.4 (CH), 127.5 (CH), 128.7 (CH), 131.6 (C), 133.9 (C), 134.0 (C), 157.8 (C) ppm. EM (CI−NH_3): *m/e* = 302 (M^+ + 1, 29), 319 (M^+ + 18, 100). Anal. Calcd for $C_{18}H_{23}NO_3$: C, 71.73%; H, 7.69%; N, 4.64%, Found: C, 72.01%; H, 7.71%; N, 4.65%.

***N*-Boc-(L)-Phenylalanine 4a.** To a solution of **10a** (50 mg, 0.2 mmol) was added under nitrogen at room temperature a solution of PDC (374 mg, 1.0 mmol) in DMF (0.75 mL). After 24 h of stirring, water (10 mL) and diethyl ether (10 mL) were added. The aqueous phase was extracted with diethyl ether (3 × 7 mL), and the combined organic phases were dried ($MgSO_4$) and evaporated. The crude product was taken with AcOEt and extracted with $NaHCO_3$ satd solution. The aqueous layer was washed with AcOEt, acidified with 2 N HCl, and extracted with AcOEt. The organic phases were then dried ($MgSO_4$) and evaporated yielding 43 mg of *N*-Boc-phenylalanine **4a** (81% yield) spectroscopically identical to a commercial sample (Propeptide). Determination of the enantiomeric purity: To a mixture of **4a** (61 mg, 0.23 mmol) and $KHCO_3$ (46 mg, 0.46 mmol) in DMF (0.4 mL) was added CH_3I (43 μL,0.69 mmol) by syringe. After 24 h of stirring water (2 mL) was added, and the aqueous phase was extracted with diethyl ether (3 × 3 mL). The combined organic phases were washed with water (2 × 2 mL), 5% aqueous Na_2SO_3 (2 × 2 mL) and brine (2 × 2 mL), dried ($MgSO_4$), and evaporated under vacuum. The crude product was chromatographed (AcOEt/hexanes 0−5%) yielding 44 mg of *N*-Boc-(L)-phenylalanine methyl ester (69% yield). Chiral HPLC analysis: only one peak at 18.9 min (> 99% ee) was observed under the following conditions: CHIRALCEL OD (25 cm) column, 30 °C, hexane/2-propanol 90/10, 0.3 mL/min, $\lambda = 254$ nm. Racemic sample: $t_R(2R) = 17.6$ min, $t_R(2S) = 19.0$ min.

***N*-Boc-(L)-(1-Naphthyl)alanine, 4b.** The procedure described in the preparation of **4a** but starting with 76 mg (0.25 mmol) of **10b** afforded 56 mg of **4b** (71% yield), spectroscopically identical to a commercial sample (Sigma). Determination of the enantiomeric purity: Chiral HPLC analysis of the methyl ester prepared as described in the preparation of **4a**. A major peak at 15.4 min (>98% ee) was observed under the following conditions: CHIRALCEL OD (25 cm) column, 30 °C, hexane/2-propanol 90/10, 0.5 mL/min, $\lambda = 254$ nm. Racemic sample: $t_R(2R) = 13.7$ min, $t_R(2S) = 15.4$ min.

(2*S*,3*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-[(*tert*-butoxycarbonyl)amino]-3-phenylbutane, 11a. To a stirred slurry of CuI (171 mg) in anhydrous diethyl ether (3 mL) at 0 °C was added MeLi (1.12 mL, 1.6 M in diethyl ether), and the mixture was stirred at this temperature several minutes. A solution of aziridine **5a** (109 mg, 0.30 mmol) in diethyl ether (3 mL) was added via cannula to the lithium dimethylcuprate solution at 0 °C, and the reaction was stirred under N_2 and monitored by TLC. When no starting material could be detected (ca. 2 h), a 8:1 mixture of saturated aqueous NH_4Cl and NH_4OH (6 mL) was added to the reaction, and the organic layer was extracted with diethyl ether (3 × 6 mL). The combined organic phases were dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography (AcOEt/hexanes 0−2%) yielding 90 mg of **11a** (80% yield) as an oil: $[\alpha]_D = -17.0$ (*c* 1.0, $CHCl_3$). IR (film): ν_{max}: 3452, 2930, 1719, 1497 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 0.048 (s, 6H), 0.92 (s, 9H), 1.27 (s, 9H), 1.39

(d, $J = 9.6$ Hz, 3H), 3.1 (m, 1H), 3.4−3.6 (m, 2H), 3.7 (m broad, 1H), 4.4 (broad s, 1H), 7.1−7.3 (m, 5H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ −5.5 (CH_3), 18.2 (C), 18.2 (CH_3), 25.9 (CH_3), 28.3 (CH_3), 39.6 (CH), 56.1 (CH), 62.8 (CH_2), 78.8 (C), 126.3 (CH), 128.2 (CH), 129.4 (CH), 143.0 (C), 154.5 (C) ppm. EM (CI−NH_3) *m/e* = 397 ($M^+ + 18$, 4), 380 ($M^+ + 1$, 100).

(2*S*,3*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-[(*tert*-butoxycarbonyl)amino]-3-(1-naphthyl)butane, 11b. To a solution of aziridine **5b** (100 mg, 0.24 mmol) in diethyl ether (2.4 mL) was added via cannula at −20 °C a solution of lithium dimethylcuprate (0.60 mmol) in diethyl ether prepared as described in the preparation of **11a**. After 4 h of stirring at this temperature, the reaction was worked up as described in the preparation of **11a** affording after chromatographic purification (AcOEt/hexanes 0.5%) 70 mg of **11b** (68% yield). $[\alpha]_D = +12.4$ (*c* 1.1, $CHCl_3$). IR (KBr) ν_{max}: 3454, 2931, 1715, 1495 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.042 (s, 3H), 0.06 (s, 3H), 0.94 (s, 9H), 1.27 (s, 9H), 1.43 (d, $J = 6.6$ Hz, 3H), 3.57−3.8 (m, 2H), 4.1 (m, 2H), 4.64 (broad d), 7.4−8.4 (m, 7H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ −5.4 (CH_3), 18.5 (CH_3), 18.3 (C), 25.9 (CH_3), 28.3 (CH_3), 33.9 (CH), 55.8 (CH), 62.8 (CH_2), 78.8 (C), 123.3 (CH), 124.1 (CH), 125.2 (CH), 125.4 (CH), 125.8 (CH), 126.7 (CH), 128.7 (CH), 132.2 (C), 133.7 (C), 139.7 (C), 155.3 (C) ppm. EM (CI−NH_3) *m/e* = 447 ($M^+ + 18$, 1), 430 ($M^+ + 1$, 100). HRMS (CI) calcd for $C_{25}H_{40}NO_3Si$ ($M^+ + 1$): 430.2777. Found: 430.2761.

(2*S*,3*S*)-2-[(*tert*-Butoxycarbonyl)amino]-3-phenylbutanol, 12a. The procedure described in the preparation of **10a**, but starting with 112 mg (0.30 mmols) of **11a**, afforded 60 mg of **12a** (80% yield) as a white solid. $[\alpha]_D = -2.3$ (*c* 1.0, $CHCl_3$). Mp 49−51 °C. IR (film) ν_{max}: 3363, 2973, 1684 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.27 (d, $J = 5.4$ Hz, 3H), 1.35 (s, 9H), 2.75 (s, broad, 1H, OH), 3.05−3.2 (m, 1H), 3.5−3.9 (m, 3H), 4.7 (broad d, 1H, NH), 7.15−7.3 (m, 5H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.3 (CH_3), 28.3 (CH_3), 40.2 (CH), 57.3 (CH), 64.0 (CH_2), 80.5 (C), 127.9 (CH), 128.5 (CH), 128.7 (CH), 142.8 (C), 156.5.0 (C) ppm. EM (CI−NH_3): *m/e* = 266 ($M^+ + 1$, 100%), 283 ($M^+ + 18$, 92%), 300 ($M^+ + 35$, 4%). Anal. Calcd for $C_{15}H_{23}NO_3$: C, 67.89%; H, 8.73%; N, 5.28%. Found: C, 67.78%; H, 8.89%; N, 5.00%.

(2*S*,3S)-2-[(*tert*-Butoxycarbonyl)amino]-3-(1-naphthyl)butanol, 12b. The procedure described in the preparation of **10a**, but starting with 115 mg (0.27 mmols) of **11b,** afforded 79 mg of **12b** as a colorless oil (93% yield). $[\alpha]_D = +29.1$ (*c* 1.1, $CHCl_3$). IR (KBr) ν_{max}: 3429, 2977, 1694, 1511 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.3 (s, 9H), 1.45 (d, $J = 6.6$ Hz, 3H), 2.3 (broad s, 1H, OH), 3.6−3.8 (m, H), 3.9−4.1 (m, 3H), 4.6 (broad s, 1H), 7.4−8.2 (m, 7H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.3 (CH_3), 28.1 (CH_3), 34.2 (CH), 57.1 (CH), 63.3 (CH_2), 79.7 (C), 123.1 (CH), 123.9 (CH), 125.3 (CH), 125.4 (CH), 126.0 (CH), 127.0 (CH), 128.9 (CH), 132.0 (CH), 133.9 (CH), 139.4 (CH), 156.0 (C) ppm. EM (CI−NH_3): *m/e* = 333 ($M^+ + 18$, 17%), 316 ($M^+ + 1$, 100%), 277 (38%), 260 (24%), 216 (6%). HRMS (CI) calcd for $C_{19}H_{25}O_3N$: 315.1834. Found: 315.1814.

(2*S*,3S)-2-[(*tert*-Butoxycarbonyl)amino]-3-phenylbutanoic Acid (*N*-Boc-(L)-*β*-Methyl-*β*-phenylalanine), 6a. The procedure described in the preparation of **4a** but starting with 114 mg (0.43 mmol) of **12b** afforded 93 mg of **6a** (77% yield), spectroscopically identical to the product described in the literature.[4] Determination of the enantiomeric purity: Chiral HPLC analysis of the methyl ester, prepared as described for **4a**: Only one peak at 20.1 min (>99% ee) was observed under the following conditions: CHIRALCEL OD (25 cm) column, 30 °C, hexane/2-propanol 90/10, 0.3 mL/min, $\lambda = 254$ nm. Racemic sample: $t_R(2R,3R) = 22.6$ min, $t_R(2S, 3S) = 20.5$ min.

(2*S*,3S)-2-[(*tert*-Butoxycarbonyl)amino]-3-(1-naphthyl)-butanoic Acid [*N*-BOC-*β*-Methyl-(L)-(1-naphthyl)alanine], 6b. The procedure described in the preparation of **4a** but starting with 53 mg (0.17 mmol) **12b** afforded 43 mg of **6b** (83% yield). $[\alpha]_D = +66.7$ (*c* 0.9, MeOH). IR (film) ν_{max}: 3051, 2979, 1717, 1600, 1397, 1163, 779 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.37 (s, 9H), 1.5 (d, $J = 6.8$ Hz, 3H), 4.2 (m, 1H), 4.65 (m, 1H), 4.9 (broad d, 1H), 7.2−7.8 (m, 7H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.4 (CH_3), 28.2 (CH_3), 35.9 (CH), 58.2 (CH), 80.5 (C), 122.8 (CH), 124.1 (CH), 125.3 (CH), 125.5 (CH), 126.2 (CH), 127.5 (CH), 128.9 (CH), 131.7 (C), 133.8 (C), 137.1 (C), 155 (C), 176 (C) ppm. EM (CI−NH_3) *m/e* = 347 ($M^+ + 18$, 100), 330 ($M^+ + 1$, 26), 291 (40). HRMS (CI) calcd for $C_{14}H_{16}NO_2$ ($M^+ -$ Boc): 230.1181. Found: 230.1190. Determination of the enantiomeric purity: Chiral HPLC analysis of the methyl ester prepared as described in the preparation of **4a**. A major peak at 31.7 min (>97% ee) was observed under the following conditions: CHIRALCEL OD (25 cm) column, 30 °C, hexane/2-propanol 99/1, 0.45 mL/min, $\lambda = 254$ nm. Racemic sample: $t_R(2R,3R) = 37.3$ min, $t_R(2S, 3S) = 31.7$ min.

Acknowledgment. Financial support from DGICYT (PB95-0265) and from CIRIT (GRQ93-1083 and 1996SGR-00013) is gratefully acknowledged. E.M. thanks Universitat de Barcelona for a predoctoral fellowship.

JO981140I