Stereoselective Reduction of Enantiopure β-Enamino Esters by Hydride: A Convenient Synthesis of Both Enantiopure β-Amino Esters

Cristina Cimarelli and Gianni Palmieri*

Dipartimento di Scienze Chimiche, via S. Agostino 1, I-62032 Camerino, Italy

Received January 17, 1996[⊗]

The reduction of enantiopure β-enamino esters **1** with sodium triacetoxyborohydride in acetic acid is described. This occurs with good diastereo- and enantioselectivity to yield β-amino esters **2** and **3** (after hydrogenolysis of the N-chiral group). A model is reported for the origin of the stereoselectivity through an enol ester−diacetoxyborohydride **6**, which affords the intramolecular reduction. By choosing the appropriate chiral amine, this procedure allows a straightforward preparation of both the enantiopure β-amino esters and derivatives with known biological activity, using readily available starting materials and inexpensive reagents and conditions.

The synthesis of enantiopure β-amino acids is an area of current interest because these compounds are crucial structural features of many biologically active compounds, as well as being found in natural products[1] and serving as key building blocks of β-lactam antibiotics.[2] With this growing interest over the past few years, several methods have been described in the literature for the synthesis of racemic compounds. Only a few methods, however, have been reported for the preparation of enantiopure β-amino acids. New procedures for their enantioselective synthesis[3] have been made by transformation of chiral pool material, by using chiral auxiliaries in the Michael additions of enantiopure lithium amides to α,β-unsaturated carboxylic acid equivalents, by addition of enantiopure enolates to imines, or by enantioselective hydrogenation of prochiral 3-aminoacrylic acid derivatives in the presence of a chiral catalyst.

During the course of our studies on the synthesis of functionalized enaminones and their reactivity,[4] we have found that β-enamino esters can be easily reduced to β-amino esters.[5] The chemoselective reduction is achieved with sodium triacetoxyborohydride in acetic acid, with the reaction showing good diastereoselectivity in the case of α-alkylated-β-enamino esters. Moreover, the reduction of enantiopure β-enamino esters **1** with this substance occurs with good diastereo- and enantioselectivity in the β-amino esters **2**.[6]

Hydrogenolizable cheap (*R*)-α-methylbenzylamine, commercially available in both enantiomeric forms, was chosen for preparing the starting β-enamino esters **1** by simple condensation with the corresponding β-keto esters.[7a−c] When these are not available, the β-enamino esters **1** can be prepared by acylation of lithium imines

[⊗] Abstract published in *Advance ACS Abstracts,* July 1, 1996.

(1) (a) Salzmann, T. N.; Ratcliffe, R. W.; Christensen, B. G.; Bonffard, F. A. *J. Am. Chem. Soc.* **1980**, *102*, 6161. (b) Drey, C. N. C. In *Chemistry and Biochemistry of the Amino Acids*; Barrett, G. C., Ed.; Chapman and Hall: London, 1985; p 25. (c) Griffith, O. W. *Ann. Rev. Biochem.* **1986**, *55*, 855. (d) Hines, J. V. *J. Org. Chem.* **1989**, *54*, 4235−4237. (e) Total and semi-synthetic approaches to Taxol. *Tetrahedron symposia-in-print* (No. 48). *Tetrahedron* **1992**, *48*, 6593. (f) Bunnage, M. E.; Burke, A. J.; Davies, S. G.; Goodwin, C. J. *Tetrahedron: Asymmetry* **1994**, *5*, 203−206. (g) Jiang, J.; Schumacher, K. K.; Jollié, M. M.; Davis, F. A.; Reddy, R.E. *Tetrahedron Lett.* **1994**, *35*, 2121−2124.

(2) (a) Dürckheimer,W; Blumbach, J.; Lattrell, R.; Scheunemann, K. H. *Angew. Chem.* **1985**, *97*, 183−205; *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 180−202. (b) Brown, M. J. *Heterocycles* **1989**, *29*, 2225−2244. (c) Hart, D. J.; Ha, D.-C. *Chem Rev.* **1989**, *89*, 1447−1465. (d) Davies, S. G.; Dordor-Hedgecock, I. M.; Jones, R. H.; Prout, K. *Tetrahedron* **1986**, *42*, 5123−5137. (e) Liebeskind, L. S.; Welker, M. E.; Fengl, R. W. *J. Am. Chem. Soc.* **1986**, *108*, 6328−6343. (f) van der Steen, F. H.; van Koten, G. *Tetrahedron* **1991**, *47*, 7503−7524. (g) Asao, N.; Tsukada, N.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1993**, 1660−1662.

(3) (a) Cole, D. C. *Tetrahedron* **1994**, *50*, 9517−9582. (b) Juaristi, E.; Quintana, D.; Escalante, J. *Aldrichim. Acta* **1994**,*27*, 3−11. (c) Davies, S. G.; Walters, I. A. S. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1129. (d) Davies, S. G.; Ichihara, O.; Walters, I. A. S. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1141. (e) Hawkins, J. M.; Lewis, T. A. *J. Org. Chem.* **1994**, *59*, 649. (f) Juaristi, E.; Escalante, J; Lamatsch, B.; Seebach, D. *J. Org. Chem.* **1992**, *57*, 2396. (g) Amoroso, R.; Cardillo, G.; Sabatino, P.; Tomasini, C.; Trerè, A. *J. Org. Chem.* **1993**, *58*, 5615. (h) Enders, D.; Klatt, M.; Funk, R. *Synlett* **1993**, 226. (i) Corey, E. J.; Decicco, C. P.; Newbold, R. C. *Tetrahedron Lett.* **1991**, *32*, 5287. (j) Hattori, K.; Miyata, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 1151. (k) Mukaiyama, T.; Akamatsu, H.; Han, J. S. *Chem. Lett.* **1990**, 889. (l) Davies, S. G.; Ichihara, O. *Tetrahedron: Asymmetry* **1991**, *2*, 183. (m) Lubell, W. D.; Kitamura, M.; Noyori, R. *Tetrahedron: Asymmetry* **1991**, *2*, 543. (n) Enders, D.; Wiedemann, J.; Bettray, W. *Synlett* **1995**, 369. (o) Enders, D.; Wahl, H.; Bettray, W. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 455.

(4) (a) Bartoli, G.; Cimarelli, C.; Palmieri, G.; Bosco, M.; Dalpozzo, R. *Synthesis* **1990**, 985. (b) Bartoli, G.; Bosco, M.; Dalpozzo, R.; Guerra, M.; Cimarelli, C.; Palmieri, G. *J. Chem. Soc., Perkin Trans. 2* **1992**, 649. (c) Bartoli, G.; Bosco, M.; Dalpozzo, R.; Cimarelli, C.; Palmieri, G. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2095. (d) Bartoli, G.; Bosco, M.; Cimarelli, C.; Dalpozzo, R.; De Munno, G.; Guercio, G.; Palmieri, G. *J. Org. Chem.* **1992**, *57*, 649. (e) Bartoli, G.; Bosco, M.; Dalpozzo, R.; Cimarelli, C.; Palmieri, G. *Tetrahedron* **1993**, *49*, 2095. (f) Bartoli, G.; Bosco, M.; Cimarelli, C.; Dalpozzo, R.; De Munno, G.; Palmieri, G. *Tetrahedron: Asymmetry* **1993**, *4*, 1651. (g) Bartoli, G.; Bosco, M.; Dalpozzo, R.; De Nino, A.; Palmieri, G. *Tetrahedron* **1994**, *50*, 9831.

(5) Bartoli, G.; Cimarelli, C.; Marcantoni, E.; Palmieri, G.; Petrini, M. *J. Org. Chem.* **1994**, *59*, 5328−5335.

(6) Bartoli, G.; Cimarelli, C.; Palmieri, G. *Tetrahedron: Asymmetry* **1994**, *5*, 1455−1458.

(7) (a) Boatman, S.; Hauser, C. R. *J. Org. Chem.* **1966**, *31*, 1785. (b) Singh, R. V.; Tandon, J. P. *J. Prakt. Chem.* **1979**, *321*, 151. (c) Baraldi P. G.; Simoni, D.; Manfredini, S. *Synthesis* **1983**, 902. (d) Bartoli, G.; Cimarelli, C.; Dalpozzo, R.; Palmieri, G. *Tetrahedron* **1995**, *51*, 8613.

(8) Kinas, R.; Pankiewicz, K.; Stec, W. J.; Farmer, P. B.; Foster, A. B.; Jarman, M. *J. Org. Chem.* **1977**, *42*, 1650.

(9) The absolute configuration of the β-amino esters **2b**,**c**,**d**,**f**,**i**,**k**,**m** was ascertained by comparison of spectroscopic data of confrontable β-amino esters of known configuration.

(10) Mokhallalati, M. K.; Pridgen, L. N. *Synth. Commun.* **1993**, *23*, 2055.

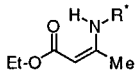
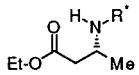
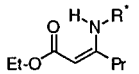
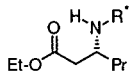
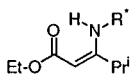
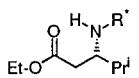
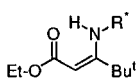
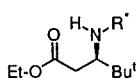
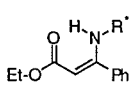
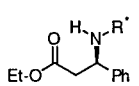
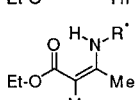
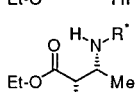
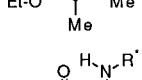
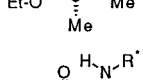
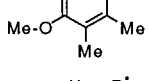
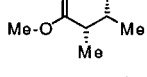
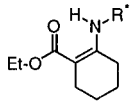
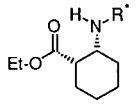
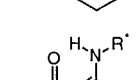
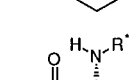
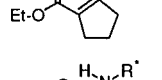
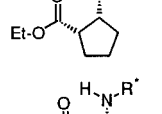
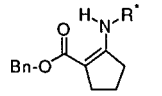
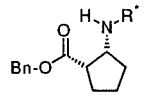
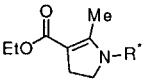
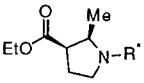
(11) Juaristi, E.; Escalante, J. *J. Org. Chem.* **1993**, *58*, 2282.

(12) The absolute configuration of the β-amino ester (*1S*,*2R*)-**2h** was ascertained by epimerization of this to (*1R*,*2R*)-**2h** [$[\alpha]^{20}_{D} = -72.1$ (*c* 2.1, EtOH)] which by hydrogenolysis give ethyl (*1R*,*2R*)-2-amino-1-cyclohexanecarboxylate [$[\alpha]^{20}_{578} = -52.9$, $[\alpha]^{20}_{365} = -112.2$ (*c* 2.7, EtOH) [lit. $[\alpha]^{20}_{578} = -42.6$, $[\alpha]^{20}_{364} = -119$ (*c* 1.08, EtOH)] (Armarego, W. L. F.; Kobayashi, T. *J. Chem. Soc. C* **1970**, 1597) and ethyl (*1S*,*2S*)-2-amino-1-cyclohexanecarboxylate [$[\alpha]^{20}_{578} = +56.3$ (*c* 0.266, EtOH)] (Armarego, W. L. F.; Kobayashi, T. *J. Chem. Soc. C* **1969**, 1635).

(13) The hydrogenolysis of the β-amino ester **2j** with $Pd(OH)_2/C$ directly gives the pure (*1S*,*2R*)-2-amino-1-cyclopentanecarboxylic acid [$[\alpha]^{20}_{D} = +8.2$ (*c* 2.3, H_2O) [lit. [$[\alpha]^{20}_{D} = -8.8$ (*c* 1.0, H_2O)]] for the (*1R*,*2S*)-2-amino-1-cyclopentanecarboxylic acid (cispentacin) (Davies, S. G.; Ichihara, O.; Walters, I. A. S. *Synlett* **1993**, 461).

S0022-3263(96)00107-7 CCC: $12.00

Table 1. Reduction of Enantiopure β-Enamino Esters 1a−m to β-Amino Esters 2a−m with $NaHB(OAc)_3$/AcOH

Entry	1	Substrate [a]	2	Product [a]	*d.e.* [b] (*syn*/*anti*)	Isolated Yeld (%) [c]	$[\alpha]^{20}_D$ [d]
1	**1a**		(3*R*)-**2a** [8]		58	61	+46.5 (c 2.3, PhH)
2	**1b**		(3*R*)-**2b** [9]		46	63	+46.2 (c 4.2)
3	**1c**		(3*S*)-**2c** [9]		30	58	+53.1 (c 2.3)
4	**1d**		(3*R*)-**2d** [9]		69	64	+18.6 (c 3.1)
5	**1e**		(3*R*)-**2e** [10]		54	72	+84.5 (c 3.6)
6	**1f**		(2*S*,3*R*)-**2f** [9]		72 (5.5)	63	+46.3 (c 1.8)
7	**1g**		(2*S*,3*R*)-**2g** [11]		70 (5.0)	54	+47.4 (c 3.8)
8	**1h**		(1*S*,2*R*)-**2h** [12]		81 (28)	73	+59.5 (c 2.8)
9	**1i**		(1*S*,2*R*)-**2i** [9]		85 (> 50)	66	+101.6 (c 4.1)
10	**1j**		(1*S*,2*R*)-**2j** [13]		67 (> 50)	71	+73.9 (c 2.3)
11	**1k**		(*RR*)-**2k** [9]		71 (14)	71	+31.1 (c 4.2)
12	**1l**		(*RR*)-**2l** [14]		74 (12)	72	+27.2 (c 2.9)
13	**1m**		(3*S*,1′*R*)-**2m** [9]		81 (1.5)	47	+44.2 (c 4.9)

[a] R* = (*R*)-α-methylbenzyl. [b] Determined by GC−MS or ^{1}H and ^{13}C NMR on the mixture reaction before purification. [c] Value refer to isolated yields of major diastereomer of >99% purity. [d] All $[\alpha]^{20}_D$ were measured for solution in 95% ethanol unless otherwise stated.

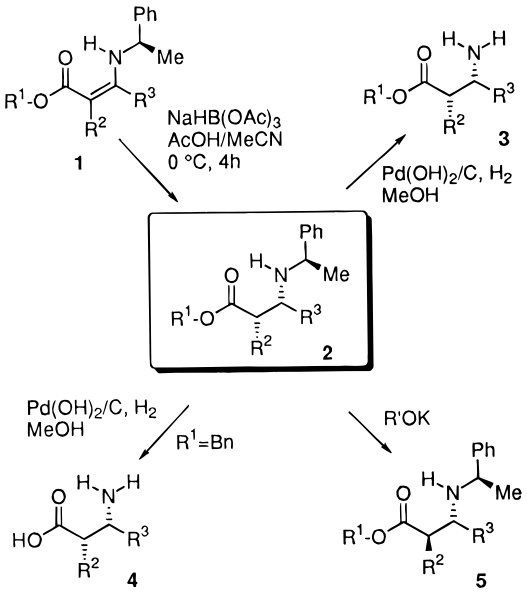
with carbonates or chloroformates.[7d] This procedure affords good yields in the isolated enantiopure β-amino esters by simple chromatographic separation of the reaction mixture (see Table 1), although moderate asymmetric inductions (de) were observed for this reaction in some entries. The reduction is fast in spite of the mild reaction conditions, easy to perform, and inexpensive, and the readily available reagents and starting materials, in both the enantiopure forms, provide a convenient asymmetric entry to both the antipodes of the β-amino esters. This procedure is not, however, suitable for β-enamino ketones (vinylogous amides), which are generally resistant to these reductive conditions because of their low basicity, yielding starting material in quantitative recovery.[15]

All the compounds show analytical and spectroscopic data in agreement with the structure reported and with the literature data. Attribution of the absolute configuration for the new β-amino esters is made by converting them into derivatives (see Scheme 1), whose absolute configuration is known in the literature, and by comparison of the $[\alpha]^{20}_D$, as reported in the respective references (see Table 1). Although the enantiopure β-amino esters **2d** and their derivatives are not reported in the literature, their absolute configuration was assigned by the correlation of the ^{1}H NMR recorded for the two isolated diastereomers and the more stable conformation assumed by the two possible stereoisomers. The $\Delta\delta$ observed in ^{1}H NMR are imputable to the shielding effect of the phenyl group on the protons at the bottom.[16]

(14) Haviari, G.; Célérier, J. P.; Petit, H.; Lhommet, G.; Gardette, D.; Gramain, J. C. *Tetrahedron Lett.* **1992**, *33*, 4311.

(15) Borch, R. F.; Bernstein, M. D.. Durst, H. D. *J. Am. Chem. Soc.* **1971**, 93, 2897.

Scheme 1



The H-3 and the *t*-Bu of (3*S*)-**2d**, at the bottom of the phenyl group (see the optimized conformation[17] depicted in Figure 1) undergo a shielding effect of $\Delta\delta = 0.27$ and 0.13 ppm, respectively, if referred to the chemical shifts of the corresponding protons recorded for (3*R*)-**2d** (see the Experimental Section). Similarly, the structure (3*S*,1′*R*)-**2m** was assigned to the major stereoisomer obtained from **1m**.

Further experimental findings are in agreement with the assignment of the (3*R*) configuration for the major diastereomer **2d**: the β-amino ester **3d**, obtained by hydrogenolysis of the major stereoisomer of **2d**, shows a $[\alpha]^{20}_{D} = +20.8$ in agreement with the optical activity shown by L-series β-amino acids.[18] In addition, the β-amino ester **3d**, if analyzed as an *N*-(1-naphthoyl) derivative over a chiral stationary phase (*S*,*S*-Whelk 01 column[19]), shows the same elution order as L-β-amino ester **3e** and an order opposite that of D-β-amino esters **3a**,**b**.

It is noteworthy that this procedure allows convenient preparation of compounds of known biological activity, such as the enantiopure pyrrolidines **2k**,**l**, which present insecticidal properties.[14] The cispentacin [(1*R*,2*S*)-2-aminocyclopentane-1-carboxylic acid], with powerful antifungal properties,[13] can be directly obtained by hydrogenolysis of the β-amino ester **2j** enantiomer obtained in entry 10 (Table 1).

The good stereoselective reduction (see Scheme 2) can be explained as follows: it proceeds through an enol ester−diacetoxyborohydride intermediate **6**, which is formed by ligand exchange between the β-enamino esters (**1**) and one of the labile acetoxy ligands.[20] The borohydride **6**, which is a stronger hydride donor than the parent triacetoxyborohydride, affords the intramolecular reduction to β-amino enol ester−borane complex **7** (for this reason, the alternative mechanism accounting for an intermolecular hydride reduction can be discarded). Finally, the borane complex **7** is destroyed by action of acetic acid. The high *syn*/*anti* diastereoselectivity observed in the case of cyclic β-enamino esters **1h**−**j** (*syn*/*anti* = 28−50, see Table 1) can be explained by taking into account that in the following protonation step acetic acid approaches the less hindered side to give the *cis*-β-amino esters **2h**−**j** through a concerted six-centered transition state. β-Enamino esters **1f**,**g**,**k**,**l**,**m** show less *syn*/*anti* diastereoselectivity because of the possible existence of a competitive and more stable conformer of the corresponding borane complex **7**, as explained elsewere.[5] The hypothesis of the boron−enol ester complex **6** as a key intermediate is confirmed by the experimental evidence that β-enamino ester **1n** (see Figure 2), obtained from tetronic acid, is inert in our reduction conditions. This can be explained by considering that, in this entry, the enone system is constrained in the *s*-*trans* geometry, so the hydrogen on **6n** is too far from the electrophilic

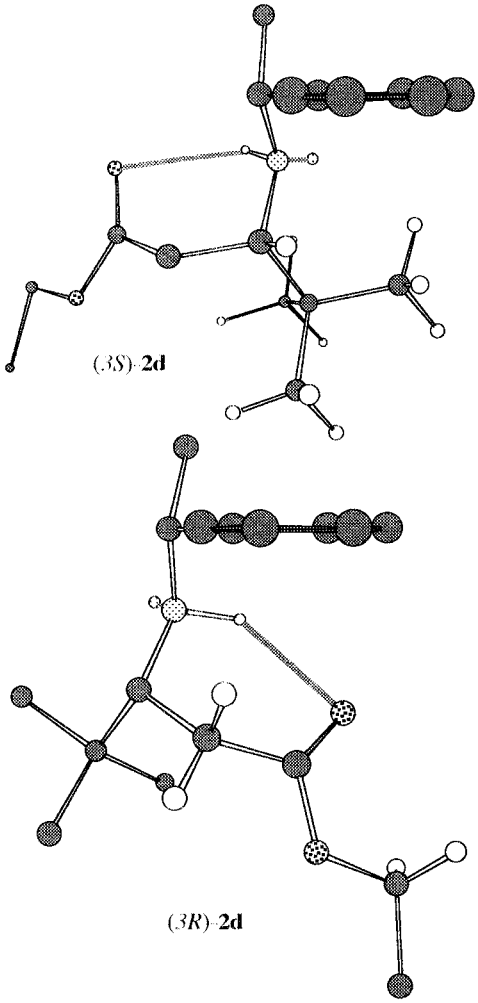


Figure 1. Optimized conformation of β-amino esters (3*S*)-**2d** and (3*R*)-**2d**. For clarity only the shielding hydrogens are reported.

(16) (a) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; Pergamon Press: Oxford, 1972. (b) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512. (c) Ohtani, I.; Kusumi, T.; Kashman, Y; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092.

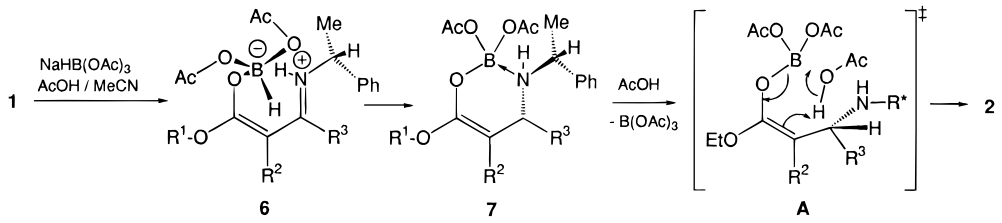
(17) The conformations were fully explored and minimized using the MM+ force field of the Hyper Chem package, from Hyper Cube Inc., Waterloo, Ontario, Canada.

(18) Generally, the α- and β-amino acids rotate polarized light in the same direction of the relative methyl or ethyl esters: (a) Jacques, J.; Gros, C.; Bourcier, S. In *Stereochemistry*; Kagan, H. B., Ed.; Georg Thieme Publishers: Stuttgart, 1977; Vol. 4, p 107. (b) Yamada, T.; Kuwata, S.; Watanabe, H. *Tetrahedron Lett.* **1978**, 1813.

(19) The β-amino esters **3a**,**b**,**d**,**e**, as *N*-1-naphthoyl derivatives, were analyzed on a *S*,*S*-Whelk 01 column (purchased from Regis Chemical Co., Morton Grove, IL), 250 × 4.6 mm i.d., hexane-isopropanol 70:30 (v/v) as eluent, UV 254 nm detector. Elution order: L before D.

(20) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560.

Scheme 2



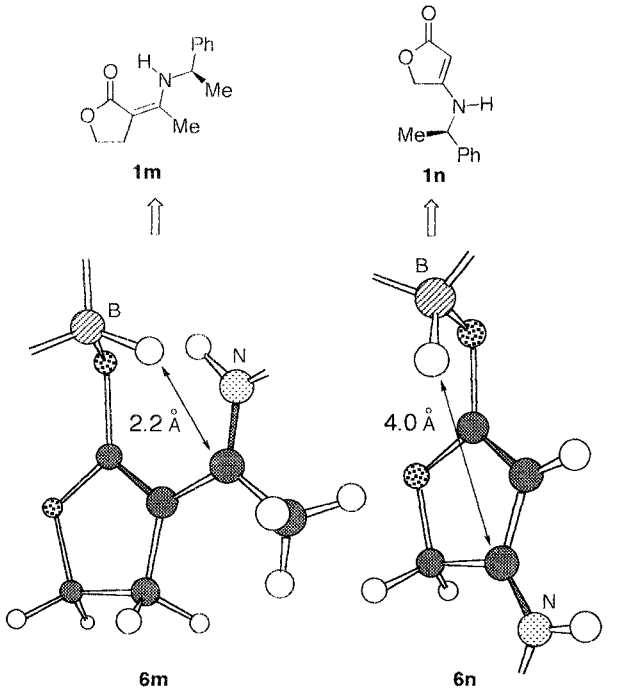


Figure 2. Comparative interaction of the BH and the electrophilic C═N groups in the *s-cis* (**6m**) and the constrained *s-trans* (**6n**) models of the intermediate enol ester−diacetoxyborohydride complexes. For clarity exemplified models were depicted.

carbon atom, if compared with the corresponding intermediate **6m** (see Figure 2).

The asymmetric induction, observed for the substrates examined, can be rationalized by examining the possible transition-state geometries for the intramolecular hydride transfer of the supposed enol ester−diacetoxyborohydride complex intermediate **6**, which is depicted in Figure 3 for the more stable conformer of **6a**. The intramolecular reduction of the immonium function of the intermediate **6a** from the front side (the less hindered diastereotopic face) affords the *β*-amino enol ester−borane complex **7a**, which upon acidolysis (AcOH), gives the *β*-amino ester **2a**. Generally, the D-*β*-amino esters **2** were obtained in agreement with the mechanism hypothesis shown. Only in the case of *β*-enamino esters **1d**,**e** were the L-*β*-amino esters (3*R*)-**2d**,**e** obtained as major stereoisomers. This exception can be explained considering that the more stable conformer for the intermediate **6d**,**e** (depicted in Figure 3 for **1e**) assumes a conformation with the bulky phenyl group remote from R^3 (Ph). Consequently, the intramolecular hydride transfer must occur on the rear side, which is the less hindered face.

The apparently anomalous enantioselectivity in the reduction of *β*-enamino esters **1k**,**l** is consistent with our mechanistic hypothesis. In the more stable conformers **6k**,**l**, the hydride transfer occurs on the less hindered *si* face (rear side, Figure 4)[14] of the electrophilic immonium function, which is constrained in the *s-trans* geometry (with respect to the enol function).

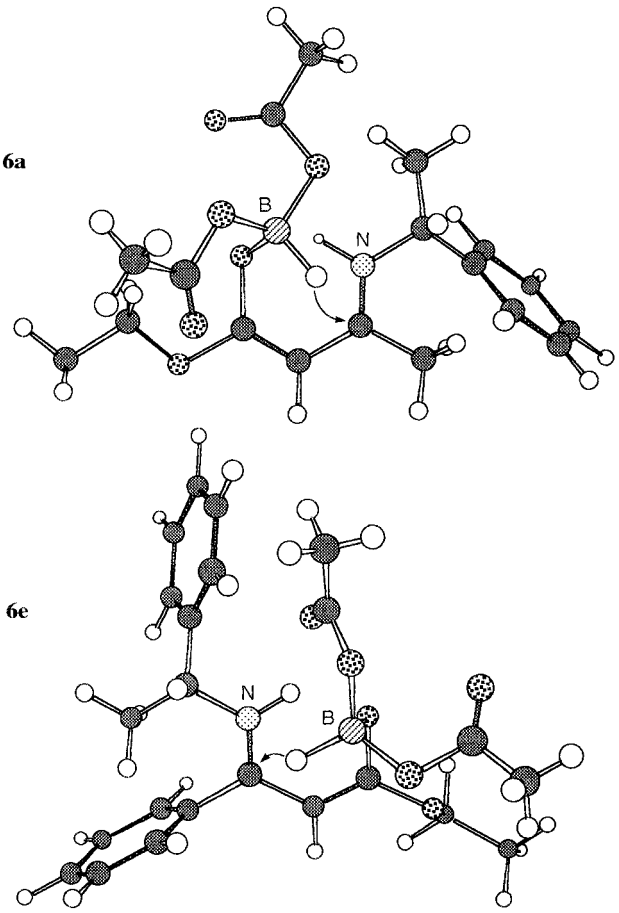


Figure 3. Hypotized, not minimized, transition-state model geometries for intramolecular hydride transfer in the case of enol ester−diacetoxyborohydride complexes **6a** (top) and **6e** (bottom, the rear view).

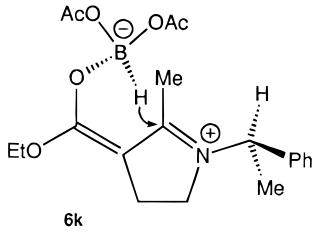


Figure 4. Possible transition state for intramolecular hydride transfer in the case of enol ester−diacetoxyborohydride complex **6k**.

Noteworthy is the trend of asymmetric induction with the bulkiness of the R^3 group in the array **1a**−**f** (see Figure 5). The de decreases with the increase in size of R^3 (from Me to i-Pr) with inversion of the direction of induction for more cumbersome groups such as Ph or

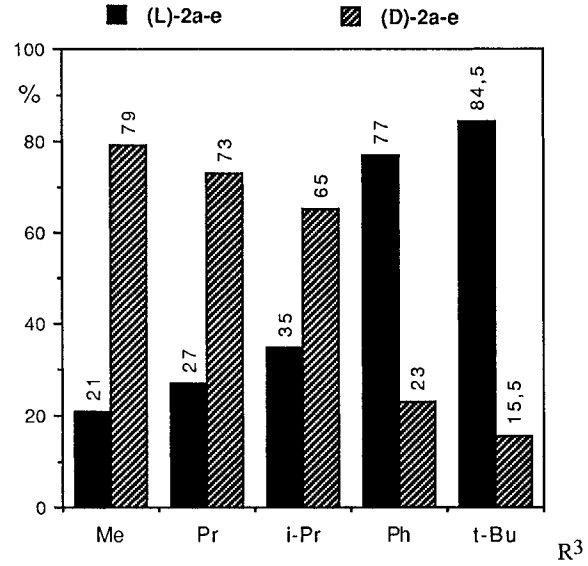


Figure 5. Trend of asymmetric induction in the reduction of β-enamino esters **1** to β-amino esters **2** with respect to the bulky of the R^3 group in the array **1a**−**e**.

t-Bu. With this increase, the **6a**-type conformation is less and less stable, if compared to the **6e**-type conformation.

To find easy access to β-amino esters with free amino function, compounds **2b**−**d**,**g**,**h**,**m** were submitted to catalytic hydrogenation (palladium hydroxide on charcoal). This widely used procedure[31] afforded the desired β-amino esters **3b**−**d**,**g**,**h**,**m** in good yields (see the Experimental Section).

In conclusion, the procedure reported is a new and convenient one for stereoselective reduction of β-enamino esters to both enantiopure β-amino esters and derivatives; the starting materials are readily available and the reagents inexpensive.

Experimental Section

General Remarks. Solvents were dried and purified according to known procedures. THF was distilled from sodium benzophenone ketyl. All reagents were distilled prior to use or were of commercial quality from freshly opened containers. All melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ solutions at 300 and 75 MHz, respectively. GLC−MS analyses were performed with a methyl silicone capillary column and by EI mass detector.

Reduction of β-Enamino Esters 1a−m to β−Amino Esters 2a−m. General Procedure. A solution of $NaBH(OAc)_3$ was prepared by adding $NaBH_4$ (0.34 g, 9.0 mmol) to glacial acetic acid (5 mL) while keeping the temperature between 10 and 20 °C. After the H_2 evolution ceased (1 h), acetonitrile (5 mL) was added and the solution was cooled to 0 °C (ice bath). The β-enamino ester (3.0 mmol) was added in one portion and the reaction stirred for 4 h at 0 °C. Evaporation of acetic acid and acetonitrile in vacuo at 50 °C followed by dissolution of the residue with CH_2Cl_2 and washing with Na_2CO_3 (saturated aqueous solution) provided the β-amino esters **2** after evaporation of the solvent. The mixture was analyzed by GC−MS or ^{1}H and ^{13}C NMR for the determination of the yields of all the diastereoisomeric β-amino esters and the de obtained. Purification and diastereoisomer separation were performed by flash chromatography or by preparative HPLC on silica gel (10−20% ethyl acetate in hexane as eluent). Yields are reported in Table 1 .

(*R*,*R*)-Ethyl 3-[*N*-(α-methylbenzyl)amino]butanoate [(*R*,*R*)-2a]: oil; $[\alpha]^{20}_D$ +46.5 (*c* 2.3, PhH); IR (film) 3300, 1730, 1190 cm^{-1}; ^{1}H NMR δ 1.05 (d, 3H, *J* = 6.4 Hz), 1.25 (t, 3H, *J* = 7.1 Hz), 1.32 (d, 3H, *J* = 6.6 Hz), 1.50 (br s, 1H), 2.35 (dd, 1H, *J* = 14.6, 6.4 Hz), 2.44 (dd, 1H, *J* = 14.6, 5.5 Hz), 2.99 (sext, 1H, *J* = 6.2 Hz), 3.88 (q, 1H, *J* = 6.6 Hz), 4.13 (q, 2H, *J* = 7.1 Hz), 7.20−7.35 (m, 5H); ^{13}C NMR δ 14.2, 21.4, 24.5, 40.9, 47.8, 55.2, 60.2, 126.5, 126.8, 128.4, 146.1, 172.3; MS *m*/*z* 235 (M^+, 1), 220 (50), 132 (31), 105 (100). Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99; N, 5.95. Found: C, 71.67; H, 9.13; N, 5.72.

(3*S*,α*R*)-Ethyl 3-[*N*-(α-methylbenzyl)amino]butanoate [(3*S*,α*R*)-2a]: oil; $[\alpha]^{20}_D$ +37.1 (*c* 1.1, EtOH); IR (film) 3300, 1720, 1180 cm^{-1}; ^{1}H NMR δ 1.06 (d, 3H, *J* = 6.2 Hz), 1.22 (t, 3H, *J* = 7.1 Hz), 1.33 (d, 3H, *J* = 6.6 Hz), 1.72 (br s, 1H), 2.28 (dd, 1H, *J* = 14.6, 5.9 Hz), 2.36 (dd, 1H, *J* = 14.6, 7.1 Hz), 2.90 (sext, 1H, *J* = 6.3 Hz), 3.91 (q, 1H, *J* = 6.6 Hz), 4.03−4.21 (m, 2H), 7.18−7.35 (m, 5H); ^{13}C NMR δ 14.7, 20.4, 25.6, 42.9, 47.5, 55.3, 60.7, 127.1, 127.3, 128.8, 145.9, 172.9; MS *m*/*z* 235 (M^+, 1), 220 (46), 132 (28), 105 (100). Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99; N, 5.95. Found: C, 71.27; H, 8.81; N, 6.13.

(3*R*,α*R*)-Ethyl 3-[*N*-(α-methylbenzyl)amino]hexanoate [(3*R*,α*R*)-2b]: oil; $[\alpha]^{20}_D$ +46.2 (*c* 4.2, EtOH); IR (film) 3340, 1725, 1180; ^{1}H NMR δ 0.80 (t, 3H, *J* = 7.0 Hz), 1.10−1.52 (m, 11H), 2.35 (dd, 1H, *J* = 14.5, 5.5 Hz), 2.46 (dd, 1H, *J* = 14.5, 5.9 Hz), 2.77 (quint, 1H, *J* = 5.8 Hz), 3.89 (q, 1H, *J* = 6.2 Hz), 4.13 (q, 2H, *J* = 7.1 Hz), 7.17−7.35 (m, 5H); ^{13}C NMR δ 14.5, 14.7, 19.6, 25.4, 38.1, 39.1, 52.3, 55.5, 60.6, 127.2, 127.3, 128.8, 146.5, 173.0; MS *m*/*z* 263 (M^+, 1), 248 (20), 105 (100). Anal. Calcd for $C_{16}H_{25}NO_2$: C, 72.97; H, 9.57; N, 5.32. Found: C, 72.81; H, 9.73; N, 5.11.

(3*S*,α*R*)-Ethyl 3-[*N*-(α-methylbenzyl)amino]hexanoate [(3*S*,α*R*)-2b]: oil; $[\alpha]^{20}_D$ +38.6 (*c* 1.9, EtOH); IR (film) 3330, 1730, 1180, 700 cm^{-1}; ^{1}H NMR δ 0.88 (t, 3H, *J* = 7.0 Hz), 1.21 (t, 3H, *J* = 7.1 Hz), 1.32 (d, 3H, *J* = 6.6 Hz), 1.15−1.60 (m, 4H), 1.70 (br s, 1H), 2.27 (dd, 1H, *J* = 15.0, 7.5 Hz), 2.36 (dd, 1H, *J* = 15.0, 5.3 Hz), 2.75−2.90 (m, 1H), 3.89 (q, 1H, *J* = 6.6 Hz), 3.97−4.21 (m, 2H), 7.15−7.35 (m, 5H); ^{13}C NMR δ 14.7, 14.8, 19.0, 25.3, 36.5, 40.4, 52.1, 55.4, 60.9, 127.2, 127.3, 128.8, 146.4, 173.1; MS *m*/*z* 263 (M^+, 1), 248 (16), 105 (100). Anal. Calcd for $C_{16}H_{25}NO_2$: C, 72.97; H, 9.57; N, 5.32. Found: C, 73.18; H, 9.78; N, 5.14.

(3*S*,α*R*)-Ethyl 3-[*N*-(α-methylbenzyl)amino-4-methylpentanoate [(3*S*,α*R*)-2c]: oil; $[\alpha]^{20}_D$ +53.1 (*c* 2.3, EtOH); IR (film) 3320, 1720, 1170 cm^{-1}; ^{1}H NMR δ 0.81 (d, 3H, *J* = 6.8 Hz), 0.88 (d, 3H, *J* = 6.8 Hz), 1.30 (t, 3H, *J* = 7.2 Hz), 1.32 (d, 3H, *J* = 6.5 Hz), 1.45 (br s, 1H), 1.68 (sept d, 1H, *J* = 6.8, 5.3 Hz), 2.34 (dd, 1H, *J* = 14.6, 6.5 Hz), 2.46 (dd, 1H, *J* = 14.6, 5.3 Hz), 2.65 (m, 1H), 3.86 (q, 1H, *J* = 6.5 Hz), 4.14 (q, 2H, *J* = 7.2 Hz), 7.17−7.43 (m, 5H); ^{13}C NMR δ 14.7, 18.9, 19.2, 25.4, 29.4, 36.4, 55.9, 58.1, 60.7, 127.2, 127.4, 128.7, 146.7, 173.5; MS *m*/*z* 263 (M^+, 1), .248 (8), 220 (99), 116 (95), 105 (100). Anal. Calcd for $C_{16}H_{25}NO_2$: C, 72.97; H, 9.57; N, 5.32. Found: C, 72.85; H, 9.72; N, 5.15.

(3*R*,α*R*)-Ethyl 3-[*N*-(α-methylbenzyl)amino]-4-methylpentanoate [(3*R*,α*R*)-2c]: oil; IR (film) 3320, 1720, 1170, 695 cm^{-1}; ^{1}H NMR δ 0.83 (d, 3H, *J* = 6.9 Hz), 0.89 (d, 3H, *J* = 6.9 Hz), 1.30 (t, 3H, *J* = 7.2 Hz), 1.32 (d, 3H, *J* = 6.5 Hz), 1.45 (br s, 1H), 1.95 (sept d, 1H, *J* = 6.8, 4.3 Hz), 2.16 (dd, 1H, *J* = 14.5, 9.0 Hz), .2.30 (dd, 1H, *J* = 14.5, 4.4 Hz), 2.77 (dt, 1H, *J* = 9.0, 4.4 Hz), 3.86 (q, 1H, *J* = 6.5 Hz), 4.20 (q, 2H, *J* = 7.2 Hz), 7.17−7.43 (m, 5H); ^{13}C NMR δ 14.7, 16.8, 19.5, 25.3, 29.5, 31.8, 55.2, 57.1, 60.7, 127.2, 127.3, 128.7, 146.4, 173.7; MS *m*/*z* 263 (M^+, 1), 248 (8), 220 (99), 116 (95), 105 (100). Anal. Calcd for $C_{16}H_{25}NO_2$: C, 72.97; H, 9.57; N, 5.32. Found: C, 72.72; H, 9.38; N, 5.09.

(3*R*,α*R*)-Ethyl 3-[*N*-(α-methylbenzyl)amino]-4,4-dimethylpentanoate [(3*R*,α*R*)-2d]: oil; $[\alpha]^{20}_D$ +18.6 (*c* 3.1, EtOH); IR (film) 3330, 1720, 1150 cm^{-1}; ^{1}H NMR δ 0.92 (s, 9H), 1.15 (t, 3H, *J* = 7.3 Hz), 1.29 (d, 3H, *J* = 6.4 Hz), 1.75 (br s, 1H), 2.13 (dd, 1H, *J* = 14.6, 6.7 Hz), 2.43 (dd, 1H, *J* = 14.6, 5.2 Hz), 2.83 (dd, 1H, *J* = 6.7, 5.2 Hz), 3.78 (q, 1H, *J* = 6.4 Hz), 3.88−4.05 (m, 2H), 7.15−7.35 (m, 5H); ^{13}C NMR δ 14.5, 24.0, 27.1, 36.9, 37.9, 57.3, 60.7, 61.7, 127.2, 127.6, 128.8, 147.6, 174.0; MS *m*/*z* 277 (M^+, 1), 262 (3), 220 (95), 116 (92), 105 (100). Anal. Calcd for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.83; H, 10.04; N, 4.87.

(3*S*,α*R*)-Ethyl 3-[*N*-(α-methylbenzyl)amino]-4,4-dimethylpentanoate [(3*S*,α*R*)-2d]: oil; $[\alpha]^{20}_D$ +78.8 (*c* 1.7, EtOH);

IR (film) 3330, 1720, 1150 cm^{-1}; ^1H NMR δ 0.79 (s, 9H), 1.25 (t, 3H, J = 7.2 Hz), 1.30 (d, 3H, J = 6.4 Hz), 1.40 (br s, 1H), 2.27 (dd, 1H, J = 13.7, 4.6 Hz), 2.51 (t, 1H, J = 5.0 Hz), 2.56 (dd, 1H, J = 13.7, 5.5 Hz), 3.80 (q, 1H, J = 6.5 Hz), 4.12 (q, 2H, J = 7.2 Hz), 7.18−7.35 (m, 5H); ^{13}C NMR δ 14.1, 25.0, 26.6, 35.1, 36.3, 56.1, 60.3, 60.8, 126.7, 127.3, 128.0, 145.8, 174.2; MS m/z 277 (M^+, 1), 262 (1), 220 (50), 105 (100). Anal. Calcd for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.52; H, 9.98; N, 5.18.

(*R*,*R*)-Ethyl 3-(*N*-(α-methylbenzyl)amino]-3-phenylpropanoate [(*R*,*R*)-2e]: oil; $[\alpha]^{20}_D$ +84.5 (*c* 3.6, EtOH); IR (film) 3340, 1735, 1180 cm^{-1}; ^1H NMR δ 1.20 (t, 3H, J = 7.14 Hz), 1.28 (d, 3H, J = 6.7 Hz), 2.18 (br s, 1H), 2.53 (dd, 1H, J = 15.2, 5.3 Hz), 2.65 (dd, 1H, J = 15.2, 9.0 Hz), 3.49 (q, 1H, J = 6.7 Hz), 3.81 (dd, 1H, J = 9.0, 5.3 Hz), 3.99−4.22 (m, 2H), 7.18−7.39 (m, 10H); ^{13}C NMR δ 14.6, 25.3, 43.5, 55.4, 57.1, 61.0, 127.3, 127.5, 127.7, 127.9, 128.9, 129.0, 142.6, 145.1, 172.1; MS m/z 297 (M^+, 1), 282 (45), 210 (67), 105 (100). Anal. Calcd for $C_{19}H_{23}NO_2$: C, 76.74; H, 7.80; N, 4.71. Found: C, 76.56; H, 7.58; N, 4.46.

(2*S*,3*R*,α*R*)-Ethyl 3-[*N*-(α-methylbenzyl)amino]-2-methylbutanoate [(2*S*,3*R*,α*R*)-2f]: oil; $[\alpha]^{20}_D$ +46.3 (*c* 1.8, EtOH); IR (film) 3350, 1735, 1190 cm^{-1}; ^1H NMR δ 0.98 (d, 3H, J = 6.6 Hz), 1.09 (d, 3H, J = 6.9 Hz), 1.28 (t, 3H, J = 7.0 Hz), 1.30 (d, 3H, J = 6.5 Hz), 1.43 (br s, 1H), 2.69 (qd, 1H, J = 6.9, 4.4 Hz), 2.74 (qd, 1H, J = 6.6, 4.4 Hz), 3.94 (q, 1H, J = 6.5 Hz), 4.16 (q, 2H, J = 7.0 Hz), 7.17−7.35 (m, 5H); ^{13}C NMR δ 13.8, 14.8, 18.6, 25.2, 43.3, 53.5, 55.5, 60.6, 127.1, 127.3, 128.9, 146.7, 175.6; MS m/z 249 (M^+, 1), 234 (32), 148 (97), 105 (100). Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.43; H, 9.42; N, 5.37.

(2*S*,3*R*,α*R*)-Methyl 3-[*N*-(α-methylbenzyl)amino]-2-methylbutanoate [(2*S*,3*R*,α*R*)-2g]: oil; $[\alpha]^{20}_D$ +47.4 (*c* 3.8, EtOH); IR (film) 3320, 1725, 1190 cm^{-1}; ^1H NMR δ 0.97 (d, 3H, J = 6.5 Hz), 1.09 (d, 3H, J = 6.9 Hz), 1.30 (d, 3H, J = 6.5 Hz), 1.45 (br s, 1H), 2.70 (qd, 1H, J = 6.9, 4.5 Hz), 2.75 (qd, 1H, J = 6.5, 4.5 Hz), 3.70 (s, 3H), 3.91 (q, 1H, J = 6.5 Hz), 7.15−7.33 (m, 5H); ^{13}C NMR δ 13.2, 18.2, 24.6, 43.1, 51.3, 53.0, 55.1, 126.5, 126.8, 128.3, 146.3, 175.6; MS m/z 235 (M^+, 1), 220 (14), 148 (72), 105 (100). Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.56; H, 8.99; N, 5.95. Found: C, 71.68; H, 9.21; N, 5.82.

(1*S*,2*R*,α*R*)-2-[*N*-(α-Methylbenzyl)amino]-1-carbethoxycyclohexane [(1*S*,2*R*,α*R*)-2h]: oil; $[\alpha]^{20}_D$ +59.5 (*c* 2.8, EtOH); IR (neat) 3340, 1720, 1175 cm^{-1}; ^1H NMR δ 1.27 (d, 3H, J = 6.5 Hz), 1.30 (t, 3H, J = 7.1 Hz), 1.35−1.95 (m, 9H), 2.70−2.88 (m, 2H), 3.87 (q, 1H, J = 6.5 Hz), 4.19 (q, 2H, J = 7.1 Hz), 7.15−7.37 (m, 5H); ^{13}C NMR δ 14.9, 23.3, 23.8, 25.1, 26.0, 30.4, 45.0, 53.9, 55.5, 60.4, 127.1, 127.2, 128.8, 147.0, 175.0; MS m/z 275 (M^+, 2), 260 (65), 120 (55), 105 (100). Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 73.91; H, 9.28; N, 5.27.

(*R*,*R*,*R*)-2-[*N*-(α-Methylbenzyl)amino]-1-carbethoxycyclohexane [(*R*,*R*,*R*)-2h]: oil; $[\alpha]^{20}_D$ −72.1 (*c* 2.1, EtOH); IR (neat) 3340, 1720, 1175 cm^{-1}; ^1H NMR δ 1.26 (d, 3H, J = 6.5 Hz), 1.30 (t, 3H, J = 7.2 Hz), 0.80−1.95 (m, 9H), 2.15 (ddd, 1H, J = 11.7, 10.2, 3.6 Hz), 2.73 (td, 1H, J = 10.2, 3.9 Hz), 3.83 (q, 1H, J = 6.5 Hz), 4.19 (q, 2H, J = 7.2 Hz), 7.15−7.37 (m, 5H); ^{13}C NMR δ 14.8, 24.4, 25.4, 25.5, 29.7, 33.8, 52.3, 56.2, 56.6, 60.6, 127.0, 127.2, 128.8, 147.6, 176.2; MS m/z 275 (M^+, 2), 260 (58), 120 (53), 105 (100). Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 73.94; H, 9.32; N, 4.87.

(1*S*,2*R*,α*R*)-2-[N-(α-Methylbenzyl)amino]-1-carbethoxycyclopentane [(1*S*,2*R*,α*R*)-2i]: oil; $[\alpha]^{20}_D$ +101.6 (*c* 4.1, EtOH); IR (neat) 3350, 1730, 1190 cm^{-1}; ^1H NMR δ 1.27 (d, 3H, J = 6.6 Hz), 1.32 (t, 3H, J = 7.1 Hz), 1.40−2.05 (m, 7H), 2.93 (td, 1H, J = 7.3, 4.8 Hz), 3.02−3.16 (m, 1H), 3.83 (q, 1H, J = 6.6 Hz), 4.20 (q, 2H, J = 7.1 Hz), 7.17−7.35 (m, 5H); ^{13}C NMR δ 14.3, 22.0, 24.9, 27.9, 32.5, 46.4, 56.6, 60.1, 60.2, 126.6, 126.7, 128.3, 146.0, 175.1; MS m/z 261 (M^+, 1), 246 (85), 120 (64), 105 (100). Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.71; H, 8.99; N, 5.19.

(1*S*,2*R*,α*R*)-2-[*N*-(α-Methylbenzyl)amino]-1-(carbobenzoxy)cyclopentane [(1*S*,2*R*,α*R*)-2j]: oil; $[\alpha]^{20}_D$ +73.9 (*c* 2.3, EtOH); IR (neat) 3300, 1720, 1150 cm^{-1}; ^1H NMR δ 1.15 (d, 3H, J = 6.6 Hz), 1.35−2.10 (m, 6H), 2.20 (br s, 1H), 3.00 (td, 1H, J = 7.3, 4.4 Hz), 3.07−3.19 (m, 1H), 3.75 (q, 1H, J = 6.6 Hz), 5.17 and 5.23 (two d, 2H, J_{AB} = 11.5 Hz), 7.23−7.49 (m, 10 H); ^{13}C NMR δ 22.5, 25.2, 28.5, 32.9, 47.0, 57.1, 60.8, 66.6, 127.1, 127.2, 128.7, 128.8, 129.0, 129.1, 136.7, 146.4, 175.4; MS m/e 323 (M^+, 1), 308 (83),105 (100). Anal. Calcd for $C_{21}H_{25}NO_2$: C, 77.99; H, 7.79; N, 4.33. Found: C, 77.73; H, 7.55; N, 4.18.

(*R*,*R*,*R*)-1-[*N*-(α-Methylbenzyl)amino]-2-methyl-3-carbethoxypyrrolidine [(*R*,*R*,*R*)-2k]: oil; $[\alpha]^{20}_D$ +31.1 (*c* 4.2, EtOH); IR (neat) 1735, 1170 cm^{-1}; ^1H NMR δ 0.82 (d, 3H, J = 6.4 Hz), 1.26 (t, 3H, J = 7.1 Hz), 1.35 (d, 3H, J = 6.5 Hz), 1.78−3.26 (m, 5H), 3.42−3.70 (m, 2H), 4.14 (q, 2H, J = 7.1 Hz), 7.20−7.40 (m, 5H); ^{13}C NMR δ 13.0, 14.8, 21.4, 25.3, 48.0, 49.3, 57.5, 60.8, 61.3, 127.4, 127.9, 128.7, 145.8, 173.6; MS m/z 261 (M^+, 10), 246 (100), 142 (77). Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.71; H, 8.95; N, 5.19.

(*R*,*R*,*R*)-1-[*N*-(α-Methylbenzyl)amino]-2-methyl-3-carbomethoxypyrrolidine [(*R*,*R*,*R*)-2l]: oil; $[\alpha]^{20}_D$ +27.2 (*c* 2.9, EtOH); IR (neat) 3300, 1715, 1155 cm^{-1}; ^1H NMR δ 0.80 (d, 3H, J = 6.4 Hz), 1.35 (d, 3H, J = 6.5 Hz), 1.80−3.60 (m, 7H), 3.67 (s, 3H), 7.18−7.39 (m, 5H); ^{13}C NMR δ 12.5, 20.9, 24.9, 47.4, 48.8, 51.5, 56.9, 60.7, 126.8, 127.4, 128.2, 145.3, 173.7; MS m/z 247 (M^+, 5), 232 (100), 105 (57). Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.97; H, 8.78; N, 5.44.

(3*S*,1′*R*,α*R*)-Dihydro-3-[1′-[*N*-(α-methylbenzyl)amino)ethyl]-2(3*H*)-furanone [(3*S*,1′*R*,α*R*)-2m]: mp 61−63 °C (CH_2Cl_2−hexane); $[\alpha]^{20}_D$ +44.2 (*c* 4.9, EtOH); IR (Nujol) 3320, 1750, 1160 cm^{-1}; ^1H NMR δ 1.02 (d, 3H, J = 6.7 Hz), 1.30 (d, 3H, J = 6.5 Hz), 1.47 (br s, 1H), 2.08−2.33 (m, 2H), 2.69 (td, 1H, J = 9.1, 3.4 Hz), 3.09 (qd, 1H, J = 6.7, 3.4 Hz), 3.87 (q, 1H, J = 6.5 Hz), 4.24 (dt, 1H, J = 8.7, 7.8 Hz), 4.36 (td, 1H, J = 7.8, 5.5 Hz), 7.18−7.35 (m, 5H); ^{13}C NMR δ 19.2, 23.9, 24.5, 43.8, 50.3, 55.7, 67.0, 126.5, 126.9, 128.4, 146.3, 178.7; MS m/z 233 (M^+, 1), 218 (55), 148 (26), 120 (36), 105 (100). Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00. Found: C, 72.19; H, 8.34; N, 5.82.

(*R*,*R*,*R*)-Dihydro-3-[1′-[*N*-(α-methylbenzyl)amino]ethyl]-2(3*H*)-furanone [(*R*,*R*,*R*)-2m]: mp 69−70 °C (CH_2Cl_2−hexane); $[\alpha]^{20}_D$ +34.1 (*c* 1.6, EtOH); IR (Nujol) 3310, 1735, 1170 cm^{-1}; ^1H NMR δ 0.94 (d, 3H, J = 6.4 Hz), 1.26 (d, 3H, J = 6.5 Hz), 1.60 (br s, 1H), 2.01−2.22 (m, 2H), 2.70 (td, 1H, J = 9.5, 5.2 Hz), 3.00 (qd, 1H, J = 6.4, 5.2 Hz), 3.76 (q, 1H, J = 6.5 Hz), 4.07 (td, 1H, J = 8.8, 7.6 Hz), 4.21 (td, 1H, J = 8.5, 4.1 Hz), 7.12−7.31 (m, 5H); ^{13}C NMR δ 17.7, 23.8, 24.4, 43.3, 50.6, 55.3, 66.8, 126.4, 126.9, 128.4, 146.0, 178.6; MS m/z 233 (M^+, 1), 218 (67), 148 (17), 120 (51), 105 (100). Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00. Found: C, 72.13; H, 8.38; N, 5.78.

Hydrogenolysis of *β*-[*N*-α-Methylbenzyl)amino] Esters 2 to *β*-Amino Esters 3. General Procedure. The *β*-amino ester **2** (3 mmol) in MeOH (20 mL), water (2 mL), and CH_3COOH (0.5 mL) in the presence of palladium hydroxide on charcoal (20%, 0.2 g) was placed under hydrogen (3 atm) and stirred at rt overnight. Then the solution was partitioned between Na_2CO_3 (saturated acqueous solution, 20 mL) and CH_2Cl_2 (100 mL) and the organic phase dried (Na_2SO_4) and filtered through a plug of Celite to provide the pure *β*-amino ester **3** in high yield after evaporation of the solvent.

Ethyl (3*S*)-3-aminohexanoate [(3*S*)-3b]: yield 86%; oil; $[\alpha]^{20}_D$= −10.7 (*c* 2.1, H_2O); IR (neat) 1450, 1190 cm^{-1}; ^1H NMR δ 0.89 (m, 3H), 1.21 (t, 3H, J = 7.2 Hz), 1.34 (m, 4H), 1.59 (br s, 2H), 2.19 (dd, 1H, J = 15.6, 8.8 Hz), 2.41 (dd, 1H, J = 15.6, 4.0 Hz), 3.13 (m, 1H), 4.10 (q, 2H, J = 7.2 Hz); ^{13}C NMR δ 13.9, 14.2, 19.1, 39.7, 42.6, 47.9, 60.2, 172.6; MS m/z 159 (M^+, 1), 130 (5), 116 (100). Anal. Calcd for $C_8H_{17}NO_2$: C, 60.35; H, 10.76; N, 8.80. Found: C, 60.48; H, 10.93; N, 8.92.

Ethyl (3*S*)-3-amino-4-methylpentanoate [(3*S*)-3c]: yield 81%; oil; $[\alpha]^{20}_D$ = −26.2 (*c* 2.3, H_2O); IR (neat) 3360, 1720, 1160 cm^{-1}; ^1H NMR δ 0.89 (d, 3H, J = 6.8 Hz), 0.90 (d, 3H, J = 6.8 Hz), 1.24 (t, 3H, J = 7.1 Hz), 1.43 (br s, 2 H), 1.60 (sept d, 1H, J = 6.8, 5.1 Hz), 2.19 (dd, 1H, J = 15.5, 9.7 Hz), 2.43 (dd, 1H, J = 15.5, 3.5 Hz), 3.00 (ddd, 1H, J = 9.7, 5.1, 3.5 Hz), 4.13 (q, 2H, J = 7.1 Hz); ^{13}C NMR δ 14.2, 17.7, 18.7, 33.4, 39.8, 53.5, 60.3, 173.0; MS m/z 159 (M^+, 2), 144 (3), 116 (100). Anal. Calcd for $C_8H_{17}NO_2$: C, 60.35; H, 10.76; N, 8.80. Found: C, 60.39; H, 10.89; N, 8.67.

Ethyl (3*R*)-3-Amino-4,4-dimethylpentanoate [(3*R*)-3d]: yield 77%; oil; $[\alpha]^{20}_D$ +20.8 (*c* 1.1, H_2O); IR (neat) 1450, 1190 cm^{-1}; ^1H NMR δ 0.0.72 (s, 9H), 1.08 (t, 3H, *J* = 7.1 Hz), 1.21 (br s, 2H), 1.92 (dd, 1H, *J* = 15.3, 10.8 Hz), 2.35 (dd, 1H, *J* = 15.3, 2.6 Hz), 2.73 (dd, 1H, *J* = 10.8, 2.6 Hz), 3.96 (q, 2H, *J* = 7.1 Hz); ^{13}C NMR δ 14.0, 25.8, 29.6, 37.6, 56.9, 60.1, 173.2; MS *m*/*z* 173 (M^+, 3), 116 (100). Anal. Calcd for $C_9H_{19}NO_2$: C, 62.39; H, 11.05; N, 8.08. Found: C, 62.27; H, 11.18; N, 8.23.

Methyl (2*S*,3*R*)-3-amino-2-methylbutanoate [(2*S*,3*R*)-3g]: yield 84%; oil; $[\alpha]^{20}_D$ +3.1 (*c* 1.1, H_2O); IR (neat) 3350, 1720, 1390 cm^{-1}; ^1H NMR δ 1.23 (d, 3H, *J* = 7.2 Hz), 1.26 (d, 3H, *J* = 6.7 Hz), 1.98 (s, 2H), 2.80 (q d, 1H, *J* = 7.2, 4.8 Hz), 3.41 (q d, 1H, *J* = 6.7, 4.8 Hz), 3.71 (s, 3H); ^{13}C NMR δ 12.8, 16.3, 42.7, 48.9, 52.1, 177.0; MS *m*/*z* 131 (M^+, 1), 116 (19), 84 (77), 56 (100). Anal. Calcd for $C_6H_{13}NO_2$: C, 54.94; H, 9.99; N, 10.68. Found: C, 55.19; H, 10.21; N, 10.52.

Methyl (2*S*,3*R*)-3-(benzoylamino)-2-methylbutanoate: mp 92 °C (CH_2Cl_2−hexane); $[\alpha]^{20}_D$ +38.7 (*c* 1.1, $CHCl_3$); IR (neat) 3300, 1720 cm^{-1}; ^1H NMR δ 1.19 (d, 3H, *J* = 6.8 Hz), 1.20 (d, 3H, *J* = 7.2 Hz), 2.77 (q d, 1H, *J* = 7.2, 4.9 Hz), 3.68 (s, 3H), 4.36 (dqd, 1H, *J* = 8.8, 6.8, 4.9 Hz), 6.98 (br d, 1H, *J* = 8.8 Hz), 7.30−7.50 (m, 3H), 7.70−7.80 (m, 2H); ^{13}C NMR δ 14.3, 17.0, 44.4, 48.0, 52.3, 127.4, 129.0, 131.9, 135.1, 167.1, 175.4; MS *m*/*z* 235 (M^+, 3), 204 (4), 148 (30), 105 (100), 77 (28). Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.49; H, 7.21; N, 5.77.

(1*S*,2*R*)-2-Amino-1-carbethoxycyclohexane [(1*S*,2*R*)-3h]: yield 74%; oil; $[\alpha]^{20}_D$ +0.9 (*c* 6.1, EtOH); IR (neat) 3350, 1730, 1180 cm^{-1}; ^1H NMR δ 1.21 (t, 3H, *J* = 7.1 Hz), 1.20−1.95 (m, 8H), 2.45−2.55 (m, 3H), 3.20−3.30 (m, 1H), 4.10 (q, 2H, *J* = 7.1 Hz); ^{13}C NMR δ 14.4, 21.2, 24.1, 24.4, 32.9, 47.3, 48.7, 60.2, 174.6; MS *m*/*z* 171 (M^+, 26), 142 (12), 56 (100). Anal. Calcd for $C_9H_{17}NO_2$: C, 63.13; H, 10.01; N, 8.18. Found: C, 63.29; H, 10.21; N, 8.02.

(*R*,*R*)-2-Amino-1-carbethoxycyclohexane [(*R*,*R*)-3h]: yield 79%; oil; $[\alpha]^{20}_D$ −52.9 (*c* 1.3, EtOH); IR (neat) 3350, 1725, 1185 cm^{-1}; ^1H NMR δ 1.22 (t, 3H, *J* = 7.1 Hz), 1.10−2.00 (m, 8H), 2.09−2.23 (m, 1H), 2.84−3.02 (m, 1H), 4.02 (br s, 2H), 4.12 (q, 2H, *J* = 7.1 Hz); ^{13}C NMR δ 14.6, 25.2, 25.5, 29.4, 34.2, 51.8, 51.8, 60.9, 175.5; MS *m*/*z* 171 (M^+, 27), 142 (12), 56 (100). Anal. Calcd for $C_9H_{17}NO_2$: C, 63.13; H, 10.01; N, 8.18. Found: C, 63.35; H, 10.16; N, 8.09.

(3*S*,1′*R*)-Dihydro-3-(1′-aminoethyl)-2(3*H*)-furanone [(3*S*,-1′*R*)-3m]: yield 71%; oil; $[\alpha]^{20}_D$ −11.0 (*c* 1.5, H_2O); IR (neat) 3360, 1750, 1160 cm^{-1}; ^1H NMR δ 1.13 (d, 3H, *J* = 6.6 Hz), 1.38 (br s, 2H), 2.09−2.42 (m, 2H), 2.60 (td, 1H, *J* = 9.8, 3.4 Hz), 3.53 (qd, 1H, *J* = 6.6, 3.4 Hz), 4.19 (td, 1H, *J* = 9.1, 7.2 Hz), 4.36 (td, 1H, *J* = 8.8, 3.2 Hz); ^{13}C NMR δ 21.2, 22.3, 45.4, 46.5, 66.8, 178.5; MS, *m*/*z* 114 (M^+-15, 54), 101 (70), 83 (57), 70 (100). Anal. Calcd for $C_6H_{11}NO_2$: C, 55.80; H, 8.58; N, 10.84. Found: C, 55.98; H, 8.77; N, 10.66.

(3*R*)-Dihydro-3-[(*R*)-1-aminoethyl]-2(3*H*)-furanone [(3*R*)-m]: yield 76%; oil; $[\alpha]^{20}_D$ +2.1 (*c* 1.3, H_2O); IR (neat) 3360, 1750, 1160 cm^{-1}; ^1H NMR δ 1.20 (d, 3H, *J* = 6.6 Hz), 1.90 (br s, 2H), 1.95−2.16 (m, 1H), 2.26−2.43 (m, 1H), 2.58 (dt, 1H, *J* = 11.4, 8.4 Hz), 3.13−3.33 (m, 1H), 4.18 (td, 1H, *J* = 10.3, 6.2 Hz), 4.35 (td, 1H, *J* = 8.6, 2.1 Hz); ^{13}C NMR δ 20.6, 26.1, 45.5, 47.8, 66.4, 178.5; MS *m*/*z* 114 (M^+ − 15, 51), 101 (62), 70 (100). Anal. Calcd for $C_6H_{11}NO_2$: C, 55.80; H, 8.58; N, 10.84. Found: C, 55.56; H, 8.69; N, 10.98.

Acknowledgment. The work was carried out with the financial support of the National Research Council (CNR) and the Ministry of the University and Scientific Research (MURST), Rome.

JO960107Y