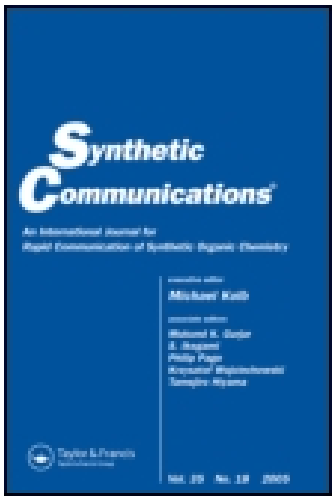

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AN IMPROVED SYNTHESIS OF ENANTIOPURE β-AMINO ACIDS

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AN IMPROVED SYNTHESIS OF ENANTIOPURE β-AMINO ACIDS

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ABSTRACT

An improved method for the preparation of both the enantiopure β-amino acids is presented. The diastereomer benzyl β-amino esters, obtained by stereoselective reduction of β-enamino esters, were separated and hydrogenolyzed to the free enantiopure β-amino acids.

The synthesis of enantiopure non-proteinogenic β-amino acids is an area of current interest because this compounds are crucial structural features of many biologically active compounds, as well as they are found in natural products[1] and serve as key building blocks for the preparation of β-lactam antibiotics[2] naturally occurring macrolides[3] and β-peptides.[4]

In the past few years several methods have been described in literature for the synthesis of racemic compounds, but only a few methods have been reported for the preparation of enantiopure β-amino acids.[5] Anyway these methods suffer of some drawbacks, as limitations in the configuration of the

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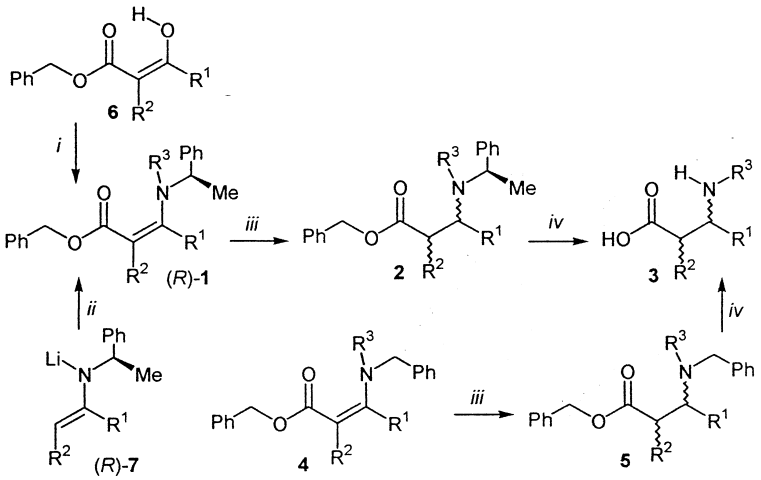

Reagents: *i* [8]; *ii* [9]; *iii* - $NaHB(OAc)_3$, AcOH, MeCN, 0 °C, 2 h; *iv* - H_2, $Pd(OH)_2/C$, MeOH, 18 h, r.t.

Scheme 1.

final product, long and complex experimental procedures, need of anhydrous reaction conditions and inert atmosphere.

During the course of our studies on the reduction of enaminones we have found that β-enamino esters can be easily and stereoselectively reduced to β-amino esters with sodium triacetoxyborohydride in acetic acid.[6] This stereoselective reductive ammination is fast, in spite of the mild reaction conditions, easy to perform and has been selected as suitable to a large scale synthesis too.[7] Moreover this method allows to prepare separately both the enantiomers of the desired product, depending on the selected enantiomer of the starting chiral amine, which is commercially available and cheap in both enantiomeric forms.

The starting β-enamino esters **1** can be easily obtained in a classical way by direct condensation[8] of (*R*)-1-phenylethylamine with the corresponding benzyl β-keto esters **6** or, when benzyl ester is not available, by acylation of lithium imines **7** with benzyl chloroformates.[9] The β-enamino ester (*R*)-**1f** was prepared by condensation of (*R*)-1-phenylethylamine with benzyl 1-acetylcyclopropanecarboxylate.[10]

In this paper we have applied the diastereoselective reduction procedure[6] on a wider range of substrates, finding a good diastereoselectivity in this case too. Moreover a high *cis* diastereoselectivity in the reduction of cyclic β-enamino esters was observed.[6] Yields and products are reported in

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Table 1. In the subsequent step the presence of a benzylic group both on ester and amino functionalities allows the easy preparation of the free β-amino acids **3** by direct and quantitative hydrogenolysis of the benzyl β-amino esters **2** and **5**. This procedure, although yet used occasionally by other researchers,[11] has not been systematically studied and used before in the preparation of β-amino acids. In our study the experimental conditions and procedures are optimized to define a routine procedure for the preparation of β-amino acids. Moreover the use of chiral (*R*)-1-phenylethylamine to prepare the starting β-enamino esters makes possible to separate the diastereoisomeric β-amino esters after the reduction step and to submit to catalytic hydrogenation only the desired pure diastereoisomer. In this way the final free β-amino acid is obtained in enantiopure form without any need of purification (Table 1; entries 1 and 2). Really, after the catalytic hydrogenation step the experimental procedure is very simple: it is enough to remove the Pearlman's catalyst by filtration and evaporate the mixture to dryness to have the desired free β-amino acids **3**. In this way the step of hydrolysis of the ester functionality is avoided, with the long, consequent and tedious workup procedure, generally used for the isolation of the final zwitterionic product **3**. The β-amino acids **3** obtained and the relative yields are reported in Table 1.

At the same time our interest was in the study of direct chromatographic resolution on a chiral stationary phase[12] to separate β-amino acids enantiomers, and we needed the corresponding raceme products to test our method. So we have applied the overall procedure to the direct preparation of (±)-β-amino acids **3** by hydrogenolysis of simple benzylamino benzyl esters (±)-**5a–f**. Our results are reported in Table 1.

In conclusion this methodology represents an improved synthesis of enantiopure β-amino acids with good overall yields, starting from ready accessible and cheap reagents and through a simple procedure of practical utility. Moreover our procedure allows to choose the suitable synthetic pathway to reach separately both the enantiomers of the desired product and makes possible the simple expeditious asymmetric synthesis of β-amino acids with biological activity too, as 2-amino cyclopentane[13] and 2-amino cyclohexane[7] carboxylic acids and derivatives.

EXPERIMENTAL SECTION

Reduction of β-Enamino Esters 1 to β-Amino Esters 2. 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), keeping temperature in the range

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Table 1. Synthesis of β-Amino Acids **3a–f** by Reduction of β-enamino Esters **1a–f** and **4a–f**

Entry	R^1	R^2	R^3	**2**, **5**	Yield[a] (%)	**3**	Yield[a] (%)
1	Me	H	H	(*R*,*R*)-**2a**[6b]	67	(*R*)-**3a**[5o]	90
2	Me	H	H	(3*S*,1′*R*)-**2a**	12[c]	(*S*)-**3a**[5o]	88
3	Me	H	H	(*S*,*S*)-**2a**	71	(*S*)-**3a**	92
4	Me	H	H	(±)-**5a**	76	(±)-**3a**	90
5	*i*-Pr	H	H	(3*S*,1′*R*)-**2b**[6b]	56	(*S*)-**3b**[5o]	91
6	*i*-Pr	H	H	(±)-**5b**	86	(±)-**3b**	93
7	Ph	H	H	(*R*,*R*)-**2c**[6b]	68	(*R*)-**3c**[14]	89
8	Ph	H	H	(±)-**5c**	89	(±)-**3c**	86
9	$-(CH_2)_3-$		H	(1*S*,2*R*,1′*R*)-**2d**[6a,b]	73	(1*S*,2*R*)-**3d**[13]	87
10	$-(CH_2)_3-$		H	*cis*-(±)-**5d**	83	*cis*-(±)-**3d**	89
11	$-(CH_2)_3-$		H	*trans*-(±)-**5d**	6	*trans*-(±)-**3d**[5n]	84
12	$-(CH_2)_4-$		H	(1*S*,2*R*,1′*R*)-**2e**[6a,b]	74	(1*S*,2*R*)-**3e**	84
13	$-(CH_2)_4-$		H	*cis*-(±)-**5e**	81	*cis*-(±)-**3e**	85
14	$-(CH_2)_4-$		H	*trans*-(±)-**5e**	7	*trans*-(±)-**3e**[5n]	83
15	Me	$-(CH_2)_2-$		(*R*,*R*,*R*)-**2f**[6a,b]	73	(*R*,*R*)-**3f**	89
16	Me	$-(CH_2)_2-$		*cis*-(±)-**5f**	79	*cis*-(±)-**3f**	88

[a]Yields of the pure isolated compound.
[b]Structure of the major stereoisomer obtained with the use of the (*R*)-(+)-phenylethylamine.
[c]Isolated as minor diastereomer in the preparation of (*R*,*R*)-**2a** (entry 1).

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10–20°C until hydrogen evolution ceased. Then acetonitrile (5 mL) was added and the solution was cooled to 0°C (ice bath). The β-enamino ester **1** or **4** (3.0 mmol) was added in one portion and the reaction mixture was stirred for 2 h at 0°C. Acetic acid and acetonitrile were evaporated in vacuo at 50°C, then the residue dissolved in CH_2Cl_2 and washed with Na_2CO_3 saturated aqueous solution. The organic layer was dried with anhydrous Na_2SO_4 and, after evaporation under reduced pressure of the solvent, β-amino ester **2** or **5** were obtained. The mixture was analysed by GC-MS or ^{1}H- and ^{13}C-NMR to determine the yields of all the diastereoisomeric β-amino esters and the *d.e.* 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).

Benzyl (3*R*)-{[(1*R*)-1-phenylethyl]amino}butanoate [(*R*,*R*)-2a]: Oil; $[\alpha]_D^{20} + 38.6$ (c = 1.1, EtOH); IR (neat) 3350, 1715, 1440, 1170 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.07 (d, 3H, $J = 6.5$ Hz), 1.32 (d, 3H, $J = 6.5$ Hz), 1.89 (br s, 1H), 2.44 (dd, 1H, $J = 4.7$, 14.7 Hz), 2.53 (dd, 1H, $J = 3.8$, 14.7 Hz), 3.03 (sext, 1H, $J = 6.2$ Hz), 3.88 (q, 1H, $J = 6.5$ Hz), 5.13 (s, 2H), 7.15–7.44 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 21.26, 24.25, 40.61, 47.94, 55.27, 66.16, 126.59, 127.02, 128.23, 128.25, 128.48, 128.54, 135.90, 171.95; MS (EI, 70 eV): *m*/*z* (%) = 297 (M^+, 1), 282 (91), 148 (38), 120 (94), 95 (96), 91 (100); Anal. Calcd. for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.80; N, 4.71. Found C, 76.96; H, 8.03; N, 4.46.

Benzyl (3*S*)-3-{[(1′*R*)-1′-phenylethyl]amino}butanoate [(3*S*,1′*R*)-2a]: Oil; $[\alpha]_D^{20} + 16.8$ (c = 1.7, EtOH); IR (neat) 3320, 1715, 1440, 1165 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.08 (d, 3H, $J = 6.3$ Hz), 1.33 (d, 3H, $J = 6.6$ Hz), 1.95 (br s, 1H), 2.37 (dd, 1H, $J = 15.5$, 5.8 Hz), 2.46 (dd, 1H, $J = 15.5$, 7.2 Hz), 2.93 (sext, 1H, $J = 6.2$ Hz), 3.92 (q, 1H, $J = 6.6$ Hz), 5.07 and 5.14 (two d, 2H, $J_{AB} = 12.3$ Hz), 7.15–7.44 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 20.31, 25.59, 42.86, 47.61, 55.36, 66.66, 127.09, 127.38, 128.75, 128.92, 129.04, 136.40, 145.66, 172.62; MS (EI, 70 eV): *m*/*z* (%) = 297 (M^+, 1), 282 (86), 148 (32), 120 (89), 95 (94), 91 (100); Anal. Calcd. for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.80; N, 4.71. Found: C, 76.83; H, 7.92; N, 4.51.

Benzyl 3-(benzylamino)butanoate [(±)-5a]: Oil; IR (neat) 3330, 1718, 1445, 1170 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.19 (d, 3H, $J = 1.2$ Hz), 2.49 (dd, 1H, $J = 15.4$, 6.2 Hz), 2.64 (dd, 1H, $J = 15.4$, 6.7 Hz), 3.21 (sext, 1H, $J = 6.4$ Hz), 3.78 and 3.89 (two d, 2H, $J_{AB} = 13.1$ Hz), 5.12 (s, 2H), 7.21–7.38 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 16.32, 38.68, 47.71, 49.34, 66.56, 128.31, 128.55, 128.81, 129.04, 129.18, 129.60, 131.77, 175.30. MS (EI, 70 eV): *m*/*z* (%) = 283 (M^+, 1), 268 (1), 192 (4), 134 (32), 106 (42), 91 (100); Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 76.30; H, 7.47; N, 4.94. Found: C, 76.47; H, 7.69; N, 5.13.

Benzyl (3*S*)-4-methyl-3-{[(1′*R*)-1′-phenylethyl]amino}pentanoate [(3*S*, 1′*R*)-2b]: Oil; $[\alpha]_D^{20} + 14.6$ (c = 1.3, EtOH); IR (neat) 3320, 1715, 1440, 1165 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.80 (d, 3H, $J = 6.8$ Hz), 0.87 (d, 3H,

$J = 6.8$ Hz), 1.28 (d, 3H, $J = 6.5$ Hz), 1.55 (br s, 1H), 1.69 (sept d, 1H, $J = 6.5$, 5.1 Hz), 2.41 (dd, 1H, $J = 14.3$, 6.6 Hz), 2.52 (dd, 1H, $J = 14.3$, 5.3 Hz), 2.70 (dt, 1H, $J = 6.5$, 5.1 Hz), 3.84 (q, 1H, $J = 6.4$ Hz), 5.14 (s, 2H), 7.15–7.48 (m, 10H); MS, m/z 325 (M^+, 2), 282 (100), 178 (93), 106 (67); Anal. Calcd. for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36; N, 4.30. Found: C, 77.32; H, 8.57; N, 4.11.

Benzyl 4-methyl-3-(benzylamino)pentanoate [(±)-5b]: Oil; IR (neat) 3325, 1720, 1440, 1165 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.90 (d, 3H, $J = 6.7$ Hz), 0.92 (d, 3H, $J = 6.7$ Hz), 1.65 (br s, 1H), 1.90 (sept d, 1H, $J = 6.7$, 4.6 Hz), 2.41 (dd, 1H, $J = 15.0$, 8.2 Hz), 2.51 (dd, 1H, $J = 15.0$, 4.6 Hz), 2.94 (dt, 1H, $J = 8.2$, 4.6 Hz), 3.78 (s, 2H), 5.14 (s, 2H), 7.15–7.41 (m, 10H); Anal. Calcd. for $C_{20}H_{25}NO_2$: C, 77.14; H, 8.09; N, 4.50. Found: C, 77.38; H, 8.32; N, 4.31.

Benzyl (3*R*)-3-phenyl-3-{[(1′*R*)-1′-phenylethyl]amino}propanoate [(*R*,*R*)-2c]: Oil; $[\alpha]_D^{20} + 53.8$ (c = 1.1, EtOH); IR (neat) 3330, 1720, 1435, 765 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.25 (d, 3H, $J = 6.6$ Hz), 1.84 (br s, 1H), 2.53–2.79 (m, 2H), 3.48 (q, 1H, $J = 6.6$ Hz), 3.80 (dd, 1H, $J = 8.8$, 5.3 Hz), 5.03 and 5.13 (two d, 2H, $J_{AB} = 12.2$ Hz), 7.10–7.40 (m, 15H); ^{13}C NMR ($CDCl_3$): δ 25.61, 43.88, 55.34, 57.11, 66.75, 127.04, 127.24, 127.31, 127.56, 127.84, 128.80, 128.84, 128.95, 129.02, 136.32, 143.09, 145.60, 171.97; MS (EI, 70 eV): m/z (%) = 359 (M^+, 1), 344 (11), 254 (13), 210 (29), 120 (29), 105 (74), 91 (100); Anal. Calcd. for $C_{24}H_{25}NO_2$: C, 80.19; H, 7.01; N, 3.90. Found: C, 79.79; H, 6.93; N, 3.81.

Benzyl 3-benzylamino-3-phenylpropanoate [(±)-5c]: Oil; IR (neat) 3320, 1715, 1440, 750 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.30 (br s, 1H), 2.71 (dd, 1H, $J = 15.5$, 5.7 Hz), 2.83 (dd, 1H, $J = 15.5$, 8.4 Hz), 3.54 and 3.66 (two d, 2H, $J_{AB} = 14.2$ Hz), 4.16 (dd, 1H, $J = 8.4$, 5.7 Hz), 5.09 (s, 2H), 7.20–7.42 (m, 15H); ^{13}C NMR ($CDCl_3$): δ 43.40, 51.68, 59.39, 66.85, 127.49, 127.72, 128.11, 128.48, 128.71, 128.86, 129.02, 129.15, 134.92, 136.21, 171.96; MS (EI, 70 eV): m/z (%) = 345 (M^+, 2), 254 (36), 196 (92), 91, (100); Anal. Calcd. for $C_{23}H_{23}NO_2$: C, 79.97; H, 6.71; N, 4.05. Found: C, 79.69; H, 6.93; N, 3.81.

Benzyl *cis*-2-(benzylamino)cyclopentane-1-carboxylate [*cis*-(±)-5d]: Oil; IR (neat) 3330, 1715, 1445, 1155 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.48–2.17 (m, 7H), 2.95–3.10 (m, 1H), 3.33 (q, 1H, $J = 6.8$ Hz), 3.74 and 3.80 (two d, 2H, $J_{AB} = 13.4$ Hz), 5.15 (s, 2H), 7.17–7.40 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 22.27, 27.47, 31.55, 47.56, 52.19, 61.38, 66.17, 126.87, 128.06, 128.15, 128.29, 128.31, 128.52, 135.92, 139.75, 174.58; MS (EI, 70 eV): m/z (%) = 309 (M^+, 2), 218 (34), 146 (57), 106 (94), 91 (100); Anal. Calcd. for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.49; N, 4.53. Found: C, 77.46; H, 7.67; N, 4.81.

Benzyl 2-(benzylamino)cyclopentanecarboxylate [*trans*-(±)-5d]: Oil; IR (neat) 3310, 1710, 1440, 1140 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.40–2.15 (m, 7H), 2.70 (q, 1H, $J = 8.0$ Hz), 3.37 (q, 1H, $J = 7.2$ Hz), 3.70 and 3.79 (two d, 2H, $J_{AB} = 13.1$ Hz), 5.10 and 5.17 (two d, 2H, $J_{AB} = 12.4$ Hz), 7.20–7.40 (m, 10H);

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^{13}C NMR ($CDCl_3$): δ 23.99, 29.18, 33.55, 51.34, 52.91, 63.23, 66.77, 127.48, 128.61, 128.63, 128.68, 128.90, 129.06, 136.55, 140.41, 175.94; Anal. Calcd. for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.49; N, 4.53. Found: C, 78.88; H, 7.33; N, 4.31.

Benzyl (1*S*,2*R*)-2-{[(1′*R*)-1′-phenylethyl]amino}cyclohexanecarboxylate (1*S*,2*R*,1′*R*)-2e: Oil; $[\alpha]_D^{20} + 48.4$ (c = 1.4, EtOH); IR (neat) 3325, 1705, 1420, 755 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.19 (d, 3H, $J = 6.5$ Hz), 1.24–1.79 (m, 9H), 2.76–2.93 (m, 2H), 3.80 (q, 1H, $J = 6.5$ Hz), 5.18 (s, 2H), 7.15–7.48 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 23.18, 23.79, 24.96, 25.90, 30.30, 45.28, 53.85, 55.52, 66.39, 127.09, 127.22, 128.66, 128.72, 128.80, 129.05, 136.79, 146.96, 174.75; MS (EI, 70 eV): m/z (%) = 337 (M^+, 2), 322 (35), 160 (26), 120 (39), 105 (100), 91 (81); Anal. Calcd. for $C_{22}H_{27}NO_2$: C, 78.30; H, 8.06; N, 4.15. Found: C, 78.09; H, 7.83; N, 3.97.

Benzyl 2-(benzylamino)cyclohexane-1-carboxylate [*cis*-(±)-5e]: Oil; IR (neat): ν = 3330, 1710, 1440, 1150 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.25–2.05 (m, 9H), 2.77 (dt, 1H, $J = 8.8$, 4.0 Hz), 3.06 (dt, 1H, $J = 6.6$, 3.6 Hz), 3.71 and 3.83 (two d, 2H, $J_{AB} = 13.2$ Hz), 5.11 and 5.16 (two d, 2H, $J_{AB} = 12.4$ Hz), 7.17–7.43 (m, 10H); ^{13}C NMR ($CDCl_3$): δ = 22.24, 24.35, 25.39, 28.93, 46.37, 51.49, 55.14, 66.46, 128.56, 128.59, 128.61, 128.63, 128.78, 129.02, 136.67, 141.08, 174.84; Anal. Calcd. for $C_{21}H_{25}NO_2$: C, 77.99; H, 7.79; N, 4.33. Found: C, 78.26; H, 7.53; N, 4.57.

Benzyl 2-(benzylamino)cyclohexanecarboxylate [*trans*-(±)-5e]: Oil; IR (neat): 3325, 1710, 1440, 1140 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.85–2.23 (m, 9H), 2.37 (ddd, 1H, $J = 11.6$, 10.3, 3.7 Hz), 2.83 (td, 1H, $J = 10.6$, 3.7 Hz), 3.71 and 3.89 (two d, 2H, $J_{AB} = 12.9$ Hz), 5.14 and 5.19 (two d, 2H, $J_{AB} = 12.4$ Hz), 7.17–7.40 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 25.29, 25.64, 29.76, 32.27, 51.21, 51.40, 58.00, 66.59, 127.31, 128.57, 128.60, 128.64, 128.81, 129.03, 136.70, 141.14, 175.85; Anal. Calcd. for $C_{21}H_{25}NO_2$: C, 77.99; H, 7.79; N, 4.33. Found: C, 78.19; H, 7.57; N, 4.14.

Benzyl (2*R*,3*R*)-2-methyl-1-[(1′*R*)-1′-phenylethyl]-3-pyrrolidinecarboxylate [(*R*,*R*,*R*)-2f]: Oil; $[\alpha]_D^{20} + 42.6$ (c = 1.8, EtOH); oil; IR (neat): ν = 1720, 1440, 1145, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$): δδ 0.80 (d, 3H, $J = 6.3$ Hz), 1.36 (d, 3H, $J = 6.3$ Hz), 1.77–3.25 (m, 4H), 3.01–3.25 (m, 1H), 3.72–3.40 (m, 2H), 5.13 (s, 2H), 7.15–7.43 (m, 10H); ^{13}C NMR ($CDCl_3$): δ = 12.91, 21.18, 25.34, 48.05, 49.23, 57.59, 61.24, 66.81, 126.99, 128.10, 128.47, 128.53, 128.71, 128.93, 136.41, 145.32, 173.44; Anal. Calcd. for $C_{21}H_{25}NO_2$: C, 77.99; H, 7.79; N, 4.33. Found: C, 77.96; H, 7.52; N, 4.51.

Benzyl *cis*-(±)-1-benzyl-2-methylpyrrolidine-3-carboxylate [*cis*-(±)-5f]: Oil; IR (neat): ν 1725, 1445, 1145, 735 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.03 (d, 3H, $J = 6.3$ Hz), 1.80–2.02 (m, 1H), 2.12–2.42 (m, 2H), 2.87–3.05 (m, 2H), 3.12 (q, 1H, $J = 8.0$ Hz), 3.38 and 3.90 (two d, 2H, $J = 13.2$), 5.13 and 5.16 (two d, 2H, $J = 12.0$), 7.18–7.41 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 14.60, 25.73, 47.37, 52.16, 57.27, 60.11, 66.27, 126.86, 128.16, 128.20, 128.40,

128.51, 128.78, 135.95, 139.04, 173.62; Anal. Calcd. for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.49; N, 4.53%. Found: C, 77.86; H, 7.34; N, 4.31%.

Hydrogenolysis of β-Amino Esters 2 and 5 to β-Amino Esters 3. General Procedure

The β-amino esters **2** or **5** (3 mmol) were dissolved in MeOH (20 mL) in the presence of palladium hydroxide on charcoal (20%, 0.2 g), then placed under hydrogen pressure (5 atm.) and stirred at r.t. overnight. After removal of the catalyst by filtration and evaporation under reduced pressure of the solvent, the pure β-amino ester **3** was obtained in 83–90% yield.

(*R*)-3-Aminobutanoic acid [(*R*)-3a]: M.p. 212–214°C (EtOH, decomp.); $[\alpha]_D^{20}$-35.6 (c = 1.6, H_2O); IR (nujol) 1573, 1458, 1392, 702 cm^{-1}; ^1H NMR (D_2O): δ = 1.19 (d, 3H, J = 6.6 Hz), 2.38 (d, 2H, J = 6.4 Hz), 3.49 (sest, 1H, J = 6.5 Hz); ^{13}C NMR (D_2O): δ = 20.54, 43.50, 48.26, 180.97; Anal. Calcd. for $C_4H_9NO_2$: C, 46.59; H, 8.80; N, 13.58. Found: C, 46.77; H, 8.96; N, 13.41.

(3*S*)-3-Amino-4-methylpentanoic acid [(*S*)-3b]: M.p. 203–205°C (EtOH, decomp.); $[\alpha]_D^{20}$-38.8 (c = 2.6, H_2O); IR (nujol) 1570, 1460, 1370, 845 cm^{-1}; ^1H NMR (D_2O): δ 0.86 (t, 3H, J = 6.8 Hz), 0.88 (t, 3H, J = 6.8 Hz), 1.82 (octet, 1H, J = 6.7 Hz), 2.27 (dd, 1H, J = 16.9, 9.1 Hz), 2.44 (dd, 1H, J = 16.9, 4.4 Hz), 3.20 (m, 1H); ^{13}C NMR (D_2O): δ 20.14, 20.31, 32.82, 38.80, 57.61, 181.23; Anal. Calcd. for $C_6H_{13}NO_2$: C, 54.94; H, 9.99; N, 10.68. Found: C, 55.21; H, 10.27; N, 10.45.

(3*R*)-3-Amino-3-phenylpropanoic acid [(*R*)-3c]: M.p. 234–237°C (EtOH, decomp.); $[\alpha]_D^{20}$ + 6.8 (c = 1.3, H_2O); IR (nujol) 1579, 1457, 1247, 696 cm^{-1}; ^1H NMR (D_2O): δ = 2.74 (dd, 1H, J = 16.1, 6.7 Hz), 2.83 (dd, 1H, J = 16.1, 7.9 Hz), 4.56 (t, 1H, J = 7.3 Hz), 7.20–7.48 (m, 5H); ^{13}C NMR (D_2O): δ = 43.39, 55.58, 129.75, 132.09, 132.25, 138.93, 180.13; Anal. Calcd. for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.62; H, 6.86; N, 8.32.

***Cis*-(1*S*,2*R*)-2-Aminocyclopentanecarboxylic acid [*cis*-(1*S*,2*R*)-3d]:** M.p. 225–227°C (EtOH, decomp.); $[\alpha]_D^{20}$ + 8.6 (c = 1.4, H_2O); IR (nujol) 1458, 1377, 1335, 845 cm^{-1}; ^1H NMR (D_2O): δ 1.53–1.81 (m, 4H), 1.87–2.09 (m, 2H), 2.73 (td, 1H, J = 8.4, 6.1 Hz), 3.59 (td, 1H, J = 6.6, 4.2 Hz); ^{13}C NMR (D_2O): δ 24.01, 30.77, 32.24, 50.39, 55.77, 183.70; Anal. Calcd. for $C_6H_{11}NO_2$: C, 55.80; H, 8.58; N, 10.84. Found: C, 55.61; H, 8.51; N, 10.62.

***Trans*-(±)-2-aminocyclopentanecarboxylic acid (*trans*-(±)-3d):** M.p. 245–248°C (EtOH, decomp.); IR (nujol) 1462, 1381, 1315, 812 cm^{-1}; ^1H NMR (D_2O): δ 1.50–1.79 (m, 4H), 1.96–2.15 (m, 2H), 2.59 (q, 1H, J = 7.7 Hz), 3.68 (q, 1H, J = 7.2 Hz); ^{13}C NMR (D_2O): δ 25.53, 32.27, 33.13, 54.47, 57.75, 184.18; Anal. Calcd. for $C_6H_{11}NO_2$: C, 55.80; H, 8.58; N, 10.84. Found: C, 55.46; H, 8.48; N, 10.78.

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***Cis*-(1*S*,2*R*)-2-aminocyclohexanecarboxylic acid [*cis*-(1*S*,2*R*)-3e]:** M.p. 220–223°C (EtOH, decomp.); $[\alpha]_D^{20} + 5.9$ (c = 1.1, H_2O); IR (nujol) 1639, 1461, 1377, 824 cm^{-1}; ^1H NMR (D_2O): δ 1.15–1.96 (m, 8H), 2.56 (dt, 1H, $J = 6.7$, 4.2 Hz), 3.37 (td, 1H, $J = 6.4$, 4.0 Hz); ^{13}C NMR (D_2O): δ 21.94, 22.42, 26.32, 27.11, 43.36, 50.12, 180.72; Anal. Calcd. for $C_7H_{13}NO_2$: C, 58.72; H, 9.15; N, 9.78. Found: C, 58.61; H, 9.24; N, 9.42.

***Trans*-(±)-2-aminocyclohexanecarboxylic acid [*trans*-(±)-3e]:** M.p. 220–223°C (EtOH, decomp.); IR (nujol) 1622, 1478, 1213, 803 cm^{-1}; ^1H NMR (D_2O): δ 1.05–2.35 (m, 8H), 2.40–2.75 (m, 1H), 3.62 (td, 1H, $J = 10.4$, 4.7 Hz); ^{13}C NMR (D_2O): δ 26.75, 27.57, 32.14, 32.59, 51.86, 55.13, 183.92; Anal. Calcd. for $C_7H_{13}NO_2$: C, 58.72; H, 9.15; N, 9.78. Found: C, 58.39; H, 9.18; N, 9.81.

(2*R*,3*R*)-2-Pyrrolidine-3-carboxylic acid [(*R*,*R*)-3f]: M.p. 215–217°C (EtOH, decomp.); $[\alpha]_D^{20}$-6.86 (c = 0.2, H_2O); IR (nujol) 1627, 1422, 781, 699 cm^{-1}; ^1H NMR (D_2O): δ 1.27 (d, 3H, $J = 6.8$ Hz), 2.00–2.23 (m, 2H), 2.94 (q, 1H, $J = 6.4$ Hz), 3.24 (dt, 1H, $J = 11.8$, 7.5), 3.47 (dt, 1H, $J = 11.8$, 8.1 Hz), 3.73 (quint, 1H, $J = 6.7$ Hz); ^{13}C NMR (D_2O): δ 15.92, 29.58, 46.82, 52.06, 60.33, 182.09; Anal. Calcd. for $C_6H_{11}NO_2$: C, 55.80; H, 8.58; N, 10.84. Found: C, 55.63; H, 8.43; N, 10.69.

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