

124. Synthesis of Enantiomerically Pure D- and L-(Heteroaryl)alanines by Asymmetric Hydrogenation of (Z)- α -Amino- α,β -didehydro Esters

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Homogeneous asymmetric hydrogenation of a wide range of methyl and *tert*-butyl (Z)-2-(acylamino)-3-(heteroaryl)acrylates (see **1a-f** and **2a-d, f, g**, resp.) catalyzed by diphosphinerhodium catalysts was studied for the synthesis of enantiomerically pure 3-furyl-, 3-thienyl-, and 3-pyrrolylalanines (see **3a-f**, and **4a-d, g**; Scheme 1). The precursors, the (Z)- α -amino- α,β -didehydro esters **1a-f** and **2a-d, f, g** were prepared in high yields using the phosphorylglycine-ester method (Scheme 1). Isomerically pure (Z)- α -amino- α,β -didehydro esters were required to obtain the highest enantiomeric excesses (ee's) in the asymmetric hydrogenation, and the *tert*-butyl-ester strategy was beneficial in terms of both getting pure (Z)- α -amino- α,β -didehydro esters and obtaining high ee's in the hydrogenation. Finally, in contrast to the methyl-ester series, deprotection of the *tert*-butyl esters **4a-d, g** was easily performed using CF₃CO₂H without any racemization.

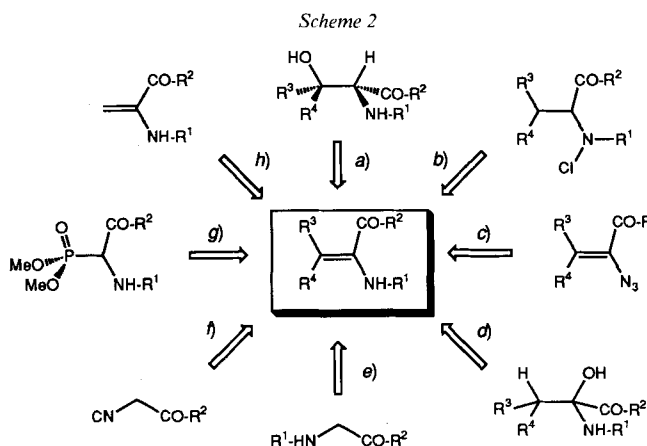
1. Introduction. – There is currently much interest in the synthesis, conformational properties, and pharmacology of α -amino acids, in particular non-coded amino acids. Consequently, several efforts focus on the development of new enantioselective methodologies for the synthesis of novel D- and L- α -amino acids with unusual side chains [1].

During the past years, numerous 'unusual' amino acids have been isolated from natural sources or synthesized by various strategies [2]. Specially designed amino acids also found interest in the field of conformational stabilization or fixation of small peptides [3]. Incorporation of 'unusual' amino acids into peptides/peptidomimetics may also provide biostability to the degradation by peptidases and, therefore, is of great interest in the design of potential therapeutic agents. In addition to these interests, non-standard amino acids are valuable tools for the creation of peptide- or non-peptide based combinatorial libraries [4]. For all these reasons, it is crucial to have a set of reliable and efficient methodologies for the synthesis of novel D- and L- α -amino acids in optically pure forms.

To date the most frequently used methods for the synthesis of enantiomerically pure amino acids include: *a*) transformations of readily available D- and L-amino acids from the chiral pool [5], *b*) the use of chiral nucleophilic or electrophilic glycine equivalents [6], *c*) enantioselective phase-transfer catalysis [7], *d*) biocatalytic or chemical resolution of racemic precursors [8], and *e*) asymmetric hydrogenation of α -amino- α,β -didehydro acids and derivatives [9]. The latter route seems especially attractive, since the transformations are highly catalytic, potentially both enantiomers are available from the same precursor, and no resolution is required. The practical utility of the asymmetric hydrogenation approach has been demonstrated by the industrial production of L-Dopa [10].

version of the phosphorylglycine ester method of *U. Schmidt* and coworkers [11]. Finally, some of the enantiomerically highly pure D- and L-alanine analogues **3** and **4** were converted in high yields by standard methods into the *N*-[(benzyloxy)carbonyl]-protected amino acids **7** and the corresponding dicyclohexylammonium salts **8**.

2. Synthesis of Methyl and *tert*-Butyl (*Z*)-2-(Acylamino)-3-(heteroaryl)acrylates (*Z*)-1** and (*Z*)-**2**, Respectively.** – Different routes to the key α -amino- $\alpha\beta$ -didehydro-acid derivatives were described in the literature (*Scheme 2*): *a*) by H_2O elimination from the corresponding α -amino- β -hydroxy-acid derivatives [12]; this method is particularly valuable when the corresponding hydroxy compound is readily accessible; *b*) by *N*-chlorination of the corresponding amino esters or acylamino ester and subsequent elimination of HCl [13]; *c*) by electrolytic reduction of α -azidoacrylates [14]; *d*) by enamine formation from α -oxo-acids or -amides [15]; *e*) by the classical *Erlenmeyer* synthesis with subsequent ring opening of the corresponding 1,3-oxazol-5(*4H*)-ones [16]; *f*) by condensation of isocynoacetates or isothiocynoacetates with carbonyl compounds, *via* formation of dihydrooxazoles or oxazolidinethiones [17]; *g*) by the phosphorylglycine ester method of *U. Schmidt* and coworkers [11]; *h*) by the *Heck* reaction from glycine derivatives, nitroacetates, and azidoacetates [18].



For the preparation of the desired furyl-, thienyl-, and pyrrolylalanine analogues **3a–f** and **4a–d, g**, we focused mainly on the construction of the corresponding aminodidehydro esters **1** and **2** using the phosphorylglycine-ester method [11] (*Scheme 1*). This approach has the following advantages over other methods: *i*) the esters (*Z*)-**1** and (*Z*)-**2** can be obtained under very mild conditions even from structurally complex and sterically hindered aldehydes; *ii*) all protecting groups can be incorporated in the starting α -amino- $\alpha\beta$ -didehydro-acid derivatives; *iii*) due to the mild reaction conditions, this approach is well suited for the synthesis of sensitive amino acids; *iv*) since the (*E/Z*)-mixtures can be efficiently isomerized to the pure (*Z*)-**1** and (*Z*)-**2**, no tedious separations are necessary.

According to the literature, the most efficient asymmetric hydrogenations with known diphosphinerhodium catalyst are performed with the pure (*Z*)- α -amino- $\alpha\beta$ -dide-

hydro-acid derivatives [19]. In some cases, the corresponding (*E*)-isomers are reduced more slowly and with much lower degree of stereoselectivity than the (*Z*)-isomers. In other cases, enantiomers with the opposite absolute configurations are obtained [20]. Our work confirms these results (see *Chapt. 3*). Thus, the synthesis of the pure (*Z*)-derivatives is a prerequisite for the successful asymmetric hydrogenations of **1** and **2**.

The methyl esters (*Z*)-**1a–f** were conveniently prepared (see *Scheme 1*) by condensation of the commercially available *rac*-methyl 2-[(benzyloxy)carbonylamino]-2-(dimethoxyphosphoryl)acetate (**6a**) with the corresponding aldehydes of type **5** in CH₂Cl₂ in the presence of *N,N,N',N'*-tetramethylguanidine (TMG) as base. This *Horner-Emmons*-type reaction gave variable mixtures of isomers (*E/Z*)-**1** (see *Table 1*). As already pointed out by *U. Schmidt* and coworkers [11], the use of a strong base such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or TMG in CH₂Cl₂ favors the formation of (*Z*)-**1** in high yield. The desired pure methyl esters (*Z*)-**1a–f** were obtained after flash chromatography (FC) [21].

Table 1. Preparation of Methyl and *tert*-Butyl α -Amino- α,β -didehydro Esters **1** and **2**, Respectively

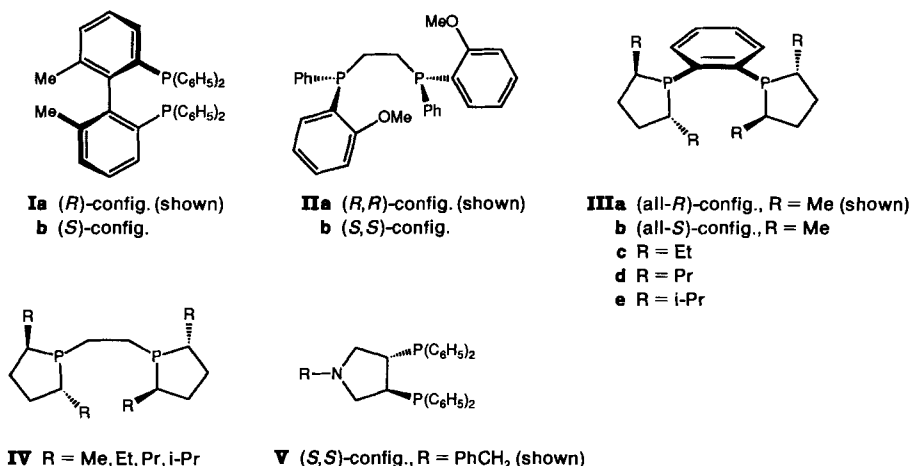
	Aldehyde	Solvent	Temp. [°C]	Product	(<i>E/Z</i>) Ratio	[%] of (<i>Z</i>)
Me Ester 6a	5a	CH ₂ Cl ₂	–30 to r.t.	1a	2:98	95.8
	5b	CH ₂ Cl ₂	–30 to r.t.	1b	2:98	91.5
	5c	CH ₂ Cl ₂	–30 to r.t.	1c	2:98	84.0
	5d	CH ₂ Cl ₂	–30 to r.t.	1d	2:98	95.2
	5e	CH ₂ Cl ₂	–30 to r.t.	1e	17:83	48
	5e	THF	–70 to r.t.	1e	17:83	56
	5f	CH ₂ Cl ₂	–30 to r.t.	1f	17:83	60
	5g	DME	–30 to r.t.	1g	13:87 ((<i>Z</i>) > 99) ^a	64.9
Bu Ester 6b	5a	CH ₂ Cl ₂	–30 to r.t.	2a	5:95 ((<i>Z</i>) > 99) ^a	86.5
	5b	CH ₂ Cl ₂	–30 to r.t.	2b	5:95 ((<i>Z</i>) > 99) ^a	87.4
	5c	CH ₂ Cl ₂	–30 to r.t.	2c	5:95 (4:96) ^a	64.8
	5d	CH ₂ Cl ₂	–30 to r.t.	2d	5:95 (4:96) ^a	81.2
	5f	CH ₂ Cl ₂	–30 to r.t.	2f	42:58	
	5f	CH ₂ Cl ₂	r.t.	2f	20:80	22
	5f	Dioxane	r.t.	2f	15:85	32
	5g	DME	–30 to r.t.	2g	13:87 ((<i>Z</i>) > 99) ^a	64.9

^a) After isomerization of (*E/Z*)-**2**.

The required racemic phosphorylglycine *tert*-butyl ester **6b** was efficiently synthesized from **6a** in 70% overall yield by selective hydrolysis (2*N* aqueous NaOH, dioxane) followed by re-esterification (see *Exper. Part*). Subsequent coupling with aldehydes **5a–d**, **f**, **g** in CH₂Cl₂ with TMG as base gave again (*E/Z*)-mixtures containing predominantly (*Z*)-**2a–d**, **f**, **g** (*Table 1*). Since the FC separation of (*E/Z*)-**2** was more tedious than for (*E/Z*)-**1**, we focused on the development of a reliable and high-yielding procedure for subsequent (*E/Z*)-isomerization: using excess TMG and charcoal, crude (*E/Z*)-**2a–d**, **f**, **g** in CHCl₃/MeOH 1:1 at room temperature was efficiently converted into almost pure (*Z*)-**2a–d**, **f**, **g**. The higher thermodynamic stability of the (*Z*)-isomers may be rationalized by the steric effects more pronounced in the *tert*-butyl-ester series than in the methyl-ester series. The *tert*-butyl esters (*Z*)-**2a–d**, **f**, **g** were simply crystallized from Et₂O/hexane in high yield, which clearly favors the use of the *tert*-butyl esters over the

methyl esters. For the coupling of *N*-Boc-protected 1*H*-pyrrole-2-carbaldehyde **5f** with **6b**, slightly harsher conditions had to be used (Table 1), and the condensation of **6b** with the 1-tosyl-protected 1*H*-pyrrole-2-carbaldehyde **5g**, which was obtained in 97% yield from **5e**, gave the desired (*Z*)-**2g** in high yield using dimethoxyethane (DME) as solvent (Table 1).

3. Asymmetric Hydrogenation of the (*Z*)-2-(Acylamino)-3-(heteroaryl)acrylates (*Z*)-1** and (*Z*)-**2**.** – The key reaction for our synthesis of optically pure D- and L-(heteroaryl)alanine is the asymmetric hydrogenation of the esters (*Z*)-**1a–f** and (*Z*)-**2a–d, g** using chiral cationic diphosphinerhodium catalysts (Scheme 1). A number of optically active *Wilkinson*-type catalysts were described for the asymmetric hydrogenation of α -amino- α,β -didehydro-acid derivatives. The most efficient Rh ligands so far described are diphosphines possessing C_2 -symmetry [22], such as, *e.g.*, compounds **I–V**.



The asymmetric hydrogenations of the esters (*Z*)-**1a–f** and **2a–d, g** were performed in MeOH using Rh complexes [Rh(cod)ligand]BF₄ (cod = cyclooctadiene) containing various chiral diphosphine ligand such as **I**, **II**, and **IIIa, b**. These complexes were prepared *in situ* by mixing the ligand with [Rh(cod)₂]BF₄ in an equimolar ratio. All hydrogenations were carried out to complete conversion at 40° under 60 bar of H₂ pressure. The ee values of the products **3a–f** and **4a–d, g** (see Tables 2 and 3) were determined by HPLC using a *Chiracel OD* column. A comparison of the results obtained by different available diphosphine ligands clearly revealed that ligands **IIa, b** [23] and **IIIa, b** [24] gave the best ee values in the asymmetric hydrogenations, **IIIa, b** being in almost all of our cases superior (highest ee values, excellent chemical yields, see Tables 2 and 3). As already described earlier, the absolute configurations of the generated α -amino-acid derivatives were very predictable by comparison with the analytical data of known compounds [25]. Thus, amino-acid derivatives of type **3** and **4** with predominantly the same (*S*)-configuration were observed with the diphosphine ligands **Ib** ((*S*)), **IIa** ((*R,R*)), **IIIb** ((all-*S*)), while the opposite (*R*)-configuration was generated using **Ia** ((*R*)), **Ib** ((*S,S*)), and **IIIa** ((all-*R*))

Table 2. *Asymmetric Hydrogenation of Methyl Esters (Z)-1*

	Ligand	[1]/[C] ^{a)}	Product	Yield [%]	ee [%]	Abs. config.
(Z)-1a	IIa (<i>R,R</i>)	1000	3a		85.5	(<i>S</i>)
	IIIb (all- <i>S</i>)	100		82.6	98.8	(<i>S</i>)
	IIIa (all- <i>R</i>)	100		99	98.4	(<i>R</i>)
(Z)-1b	Ia (<i>R</i>)	100	3b		12	(<i>R</i>)
	IIa (<i>R,R</i>)	1000			91	(<i>S</i>)
	IIIb (all- <i>S</i>)	100		97	97.5	(<i>S</i>)
(Z)-1c	IIIa (all- <i>R</i>)	100	3c	96	97.9	(<i>R</i>)
	IIa (<i>R,R</i>)	1000			90.5	(<i>S</i>)
	IIIb (all- <i>S</i>)	100		99	98.1	(<i>S</i>)
(Z)-1d	IIIa (all- <i>R</i>)	100	3d	93.5	98.0	(<i>R</i>)
	IIa (<i>R,R</i>)	1000			90.0	(<i>S</i>)
	IIIb (all- <i>S</i>)	100		99	96.5	(<i>S</i>)
(Z)-1e	IIIa (all- <i>R</i>)	100	3e	98	96.5	(<i>R</i>)
	IIIb (all- <i>S</i>)	500			96.5	(<i>S</i>)
	IIIb (all- <i>S</i>)	1000			96.2	(<i>S</i>)
(Z)-1f	IIIb (all- <i>S</i>)	100	3f	62.2	94.5	(<i>S</i>)
	IIIa (all- <i>R</i>)	100			94.5	(<i>R</i>)
(Z)-1'f ^{b)}	IIIb (all- <i>S</i>)	100	3'f ^{b)}	97.4	97.2	(<i>S</i>)
	IIa (<i>R,R</i>)	100		45.8	100 ^{c)}	(<i>S</i>)
	IIIb (all- <i>S</i>)	100		62.0	98.8 ^{c)}	(<i>S</i>)

^{a)} [1]/[C] = Molar ratio; C = catalyst.^{b)} See *Formulae 1b* and *3b*, resp., with R' = H.^{c)} % Conversion.Table 3. *Asymmetric Hydrogenation of tert-Butyl Esters (Z)-2*

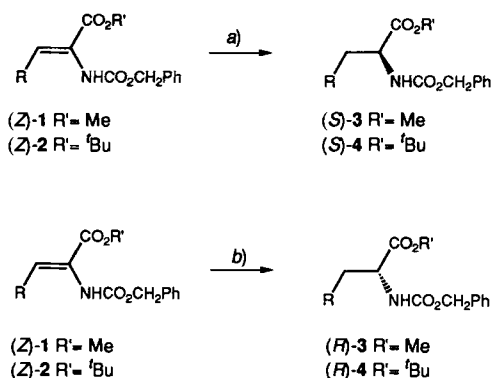
	Ligand	[2]/[C] ^{a)}	Product	Yield [%]	ee [%]	Abs. config.
(Z)-2a	IIIb (all- <i>S</i>)	100	4a	97.5	99.5	(<i>S</i>)
	IIIa (all- <i>R</i>)	100		80.0	99.6	(<i>R</i>)
(Z)-2b	IIIb (all- <i>S</i>)	100	4b	90.0	98.9	(<i>S</i>)
	IIIa (all- <i>R</i>)	100		91.5	98.4	(<i>R</i>)
(Z)-2c	IIIb (all- <i>S</i>)	100	4c	96.5	99.0	(<i>S</i>)
	IIIa (all- <i>R</i>)	100		98.5	99.1	(<i>R</i>)
(<i>E</i>)-2c	IIIb (all- <i>S</i>)	100			62.6	(<i>S</i>)
(<i>E/Z</i>)-2c (15:85)	IIIb (all- <i>S</i>)	100			91.4	(<i>S</i>)
(Z)-2d	IIIb (all- <i>S</i>)	100	4d	99.5	98.4	(<i>S</i>)
	IIIa (all- <i>R</i>)	100		99.5	98.4	(<i>R</i>)
(Z)-2g	IIIb (all- <i>S</i>)	100	4g	90.5	99.1	(<i>S</i>)
	IIIa (all- <i>R</i>)	100		95.2	98.5	(<i>R</i>)

^{a)} [2]/[C] = Molar ratio; C = catalyst.

with identical enantiomeric excess (*Scheme 3*). In addition, we observed lower ee values for the asymmetric hydrogenation of the corresponding free (*Z*)-2-[(benzyloxy)carbonyl]-3-(furan-3-yl)acrylic acid (**1'f**; see **1b**, with R' = H; *Table 2*).

To confirm that the pure (*Z*)- α -amino- α,β -didehydro esters gave the best results in the asymmetric hydrogenations, both in terms of reaction rate and in terms of enantioselectivity, we compared the asymmetric hydrogenations of (*E*)- and (*Z*)-**2c** using **IIIb**

Scheme 3



a) H₂, MeOH, 40°, 60 bar, [Rh(cod)L*]BF₄; L* = **Ib** (*S*), **IIa** (*R,R*), **IIIb** (all-*S*). b) H₂, MeOH, 40°, 60 bar, [Rh(cod)L*]BF₄; L* = **Ia** (*R*), **IIb** (*S,S*), **IIIa** (all-*R*).

under the same conditions. We obtained (*S*)-**4c** with 62.6% ee from (*E*)-**2c** and 99.0% ee from the (*Z*)-**2c** (Table 3). This result underscores the importance of having the pure (*Z*)-isomers as starting materials. It is interesting to note that in all cases investigated so far the *tert*-butyl esters (*Z*)-**2** gave consistently slightly better ee values (98.4–99.5% ee) than the corresponding methyl esters (*Z*)-**1** (94.5–98% ee) (Tables 2 and 3).

4. Cleavage of the C-Terminal Protecting Groups. – The C-terminal deprotection of the hydrogenation products **3** were achieved by mild saponification using LiOH in THF/MeOH/H₂O 3:1:1 and of **4** by treatment with aqueous CF₃CO₂H solution (Scheme 1). We observed a slight racemization during the saponification of the methyl esters **3b** and **3d** to the corresponding acid **7b** and **7d**, respectively (Table 4). However, enantiomer-

Table 4. Deprotection of the C-Terminal Protecting Group of **3** and **4**

	Reagent	Product	Yield [%]	ee [%]
(<i>S</i>)- 4b	CF ₃ CO ₂ H	(<i>S</i>)- 7b	79.5	99.1
(<i>R</i>)- 4b	CF ₃ CO ₂ H	(<i>R</i>)- 7b	82.5	98.6
(<i>S</i>)- 4c	CF ₃ CO ₂ H	(<i>S</i>)- 7c	87.2	99.4
(<i>R</i>)- 4c	CF ₃ CO ₂ H	(<i>R</i>)- 7c	83.7	98.9
(<i>S</i>)- 4d	CF ₃ CO ₂ H	(<i>S</i>)- 7d	90.5	99.8
(<i>R</i>)- 4d	CF ₃ CO ₂ H	(<i>R</i>)- 7d	89.0	99.5
(<i>S</i>)- 4g	CF ₃ CO ₂ H	(<i>S</i>)- 7g	76.8	99.0
(<i>R</i>)- 4g	CF ₃ CO ₂ H	(<i>R</i>)- 7g	82.6	99.0
(<i>S</i>)- 4a	CF ₃ CO ₂ H	(<i>S</i>)- 7a	93.7	99.5 (99.8) ^{b)}
(<i>S</i>)- 3a	LiOH	(<i>S</i>)- 7a	95.9	97.4 (99.2) ^{b)}
(<i>R</i>)- 4a	CF ₃ CO ₂ H	(<i>R</i>)- 7a	79.0 ^{a)}	98.9 (99.3) ^{b)}
(<i>R</i>)- 3a	LiOH	(<i>R</i>)- 7a	64.5 ^{a)}	97.6 (99.1) ^{b)}
(<i>S</i>)- 3b	LiOH	(<i>S</i>)- 7b	26.0 ^{a)}	95.6 (99.5) ^{b)}
(<i>S</i>)- 3d	LiOH	(<i>S</i>)- 7d	77.9 ^{a)}	95.5 (98.9) ^{b)}

^{a)} Yield of the corresponding salt **8**.

^{b)} Values in parentheses obtained from the corresponding salt **8**.

ically pure compounds (ee > 99%) were obtained by formation and recrystallization of the corresponding dicyclohexylammonium salts **8b** and **8d**. By contrast, the mild acidic cleavage of the *tert*-butyl esters **4a–d**, **g** to the corresponding acids **7a–d**, **g** proceeded without any detectable racemization. In this series, it was not necessary to form the corresponding dicyclohexylammonium salts **8**, except in the case of **7a** where purification by crystallization or alternative methods was not possible.

Conclusion. – We have developed a short and efficient synthesis of optically pure (*R*)- and (*S*)-3-(heteroaryl)alanines of type **7** and **8** (Scheme 1). The present approach combines the efficiency of the phosphorylglycine-ester method, which gave the *N*-benzyloxy-carbonyl-protected (*Z*)- α -amino- $\alpha\beta$ -didehydro esters (*Z*)-**1** and (*Z*)-**2** in high yields, with the highly enantioselective asymmetric hydrogenations using a Rh catalyst with optically pure diphosphines **I–III** as ligands, **IIIa** and **IIIb** clearly showing the most promising result.

The synthesis of pure *tert*-butyl esters (*Z*)-**2** and their asymmetric hydrogenations are described for the first time. The use of the *tert*-butyl esters (*Z*)-**2** rather than the methyl esters (*Z*)-**1** offers the following advantages: *a*) The *Horner-Emmons*-type condensation of the *tert*-butyl phosphorylglycinate **6b** with the corresponding aldehydes **5** affords, after (*E/Z*)-isomerization with TMG/charcoal, the pure *tert*-butyl esters (*Z*)-**2**, without intermediate chromatographic separations (Table 1). *b*) The asymmetric hydrogenation of the *tert*-butyl esters (*Z*)-**2**, using the ligands **IIIa** and **IIIb** generally gives higher ee values for the amino-acid derivatives **4**, as compared to those obtained for **3** from the corresponding methyl esters (*Z*)-**1** (see Tables 2 and 3). *c*) The conversion of the *tert*-butyl esters **4** into the corresponding free acids **7** (Scheme 1) using aqueous CF₃CO₂H proceeds without racemization, in contrast to the saponification of the corresponding methyl esters **3**.

The interesting properties of compounds such as **3**, **4**, **7**, and **8** have attracted the attention of numerous research groups, thus the description of these new products or of new synthetic procedures to obtain them is the subject of continuous interest [26]. Nonetheless, as already mentioned, until now no asymmetric synthesis has given consistently the desired enantiomer with ee's higher than 98%. We now have described a versatile synthetic route which is most efficient both in terms of obtaining very high ee's as well as getting good yields. The very mild reaction conditions used in this approach lends itself to the design and synthesis of novel *unusual* amino acids. Further applications of the present strategy will be described in due course.

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Experimental Part

General. All reactions with air- or moisture-sensitive reactants and solvents were carried out in oven- or flame-dried glassware under a positive pressure of dry Ar. Reaction solvents and liquid reagents were purified before use. MeOH was distilled under Ar, THF from Na with benzophenone ketyl as indicator, CH_2Cl_2 from powdered CaH_2 , and dimethoxymethane (DME) from Na and kept over 4-Å molecular sieves. All other reactants were reagent-grade unless described otherwise. Anal. TLC: 2.5×10 cm precoated TLC plates, SiO_2 60F-254, layer thickness 0.25 mm (E. Merck & Co., Darmstadt, Germany). Flash chromatography (FC): E. Merck SiO_2 60 (70–230 mesh ASTM); according to [21]. HPLC: column Chiracel OD, 250×4.6 mm; detection at 220 nm; hexane/EtOH 95:5, 1 ml/min. M.p.: Büchi-SMP-20 apparatus; uncorrected. $[\alpha]_D^{25}$: Perkin-Elmer 241 polarimeter; in CDCl_3 , at r.t. $\pm 2^\circ$, unless otherwise specified. IR Spectra: Nicolet-7199-FT spectrophotometer; solids in KBr pellets, liquids as thin films; characteristic bands in cm^{-1} . $^1\text{H-NMR}$ Spectra: Bruker-AC-250 apparatus, at 250 MHz; in DMSO or CDCl_3 ; TMS as internal standard; chemical shift of signal centers and ranges in ppm (δ), J in Hz. MS: Finnigan MS9-AEI or Mat90; m/z (rel.-%).

Methyl Esters 1: Method A. To a soln. of rac-methyl 2-[(benzyloxy)carbonylamino]-2-(dimethoxyphosphoryl)-acetate (**6a**; 1.1 mmol) in the appropriate solvent (5 ml; see Table 1) was added *N,N,N',N'*-tetramethylguanidine (TMG; 1.05 mmol) at r.t. After 15 min, the mixture was cooled to -30° and the aldehyde **5** (1 mmol) added dropwise. The mixture was then kept at -30° for 30 min; slowly allowed to come to r.t. The soln. was diluted with AcOEt (20 ml) and washed with 1N aq. KHSO_4 soln. (10 ml). The combined org. layer was washed with brine (10 ml), dried (Na_2SO_4), and evaporated: (*E/Z*)-**1**. The residue was chromatographed (SiO_2 , AcOEt/hexane 1:4 to 2:1): (*Z*)-**1**.

tert-Butyl Esters 2: Method B. According to Method A with rac-tert-butyl 2-[(benzyloxy)carbonylamino]-2-(dimethoxyphosphoryl)acetate **6b** instead of **6a** in the appropriate solvent (5 ml; Table 1) was added TMG (1.05 mmol) at r.t. After evaporation the residual (*E/Z*)-**2** was dissolved in $\text{CHCl}_3/\text{MeOH}$ 1:1 (5 ml), and charcoal (500 ml) and TMG (1.05 mmol) were added under ice-bath cooling. The mixture was stirred until total (*E*) $\rightarrow$ (*Z*) isomerization was observed. The suspension was filtered over Celite, the filtrate diluted with AcOEt (20 ml) and washed with 1N aq. KHSO_4 soln. (10 ml), the combined org. layer washed with brine (10 ml), dried (Na_2SO_4), and evaporated, and the residue was chromatographed (SiO_2 , AcOEt/hexane 1:3): (*Z*)-**2**. White solids.

The starting **6b** [27] was obtained from **6a**: To a soln. of **6a** (0.09 mol) in dioxane (65 ml) was added 2N aq. NaOH soln. (45 ml) under vigorous stirring. The solvent was removed, the remaining aq. soln. washed with AcOEt, and the aq. layer acidified with 2N aq. HCl soln. and extracted with AcOEt. The combined org. layer was washed with H_2O , and brine, dried (Na_2SO_4), filtered, and evaporated. To the residue in CH_2Cl_2 (100 ml), were added 4-(dimethylamino)pyridine (1.45 g) and *t*-BuOH (0.28 mol). The soln. was cooled to 0° , and dicyclohexylcarbodiimide (0.14 mol) was added in small portions. The mixture was allowed to come to r.t. and stirred until consumption of the acid (TLC monitoring), the precipitated urea filtered off, and the filtrate evaporated. The residue was chromatographed (SiO_2 , AcOEt/hexane 7:3): **6b**, overall yield 69.8%.

Asymmetric Hydrogenations of the (*Z*)-1 and (*Z*)-2: Method C. The complexes $[\text{Rh}(\text{cod})\text{ligand}]\text{BF}_4$ were prepared *in situ* by mixing the ligand **I**, **II**, or **IIIa**, **b** in MeOH with $[\text{Rh}(\text{cod})_2]\text{BF}_4$ in an equimolar ratio (exclusion of O_2 : all operations in glove-box). The soln. of the (*Z*)-**1** or (*Z*)-**2** (0.66 mmol) in MeOH (5 ml) and the freshly prepared catalyst soln. (0.0066 mmol) were hydrogenated in a 100-ml autoclave at $40^\circ/60$ bar overnight. The mixture was cooled and evaporated. The residue was suspended in Et_2O and filtered through a plug of SiO_2 with Et_2O . The filtrate was evaporated and the residual mixtures chromatographed (SiO_2 , AcOEt/hexane 1:3 to 1:1): **3** or **4**, resp. (Tables 2 and 3).

Salts 8: Method D. To a soln. of **3** (2.5 mmol) in THF/MeOH/ H_2O 3:1:1 (25 ml) was added at once LiOH. H_2O (3.78 mmol) under ice-bath cooling. The mixture was allowed to come to r.t. under vigorous stirring. After consumption of **3**, the mixture was evaporated, the aq. soln. acidified with 1N aq. HCl and extracted with AcOEt, and the combined org. layer washed with H_2O , and brine, dried (Na_2SO_4), and evaporated. The residue was dissolved in hot Et_2O , dicyclohexylamine (2.72 mmol) was added, and the mixture stirred. The salt **8** was then filtered off and recrystallized from MeCN (see Table 4).

Benzyloxycarbonyl-amino Acids 7: Method E. A soln. of **4** (1.7 mmol) in $\text{CH}_2\text{Cl}_2/\text{H}_2\text{O}$ 9:0.3 (18.6 ml) was treated with $\text{CF}_3\text{CO}_2\text{H}$ (3.1 ml) under ice-bath cooling. The mixture was allowed to come to r.t. under vigorous stirring, then quenched with H_2O and extracted with CHCl_3 , the combined org. layer washed with brine, dried (Na_2SO_4), filtered, and evaporated, and the residue crystallized from Et_2O /hexane 1:3: **7**.

Methyl (*Z*)-2-[(Benzyloxy)carbonylamino]-3-(furan-2-yl)prop-2-enoate ((*Z*)-1a**).** From furan-2-carbaldehyde (**5a**; Fluka; 1.8 ml, 21 mmol) in CH_2Cl_2 according to Method A: 6.1 g (95.8%) of (*Z*)-**1a**. M.p. 104° . IR (KBr):

3295m, 3063w, 1731s, 1688s, 1623s, 1564w, 1511s, 1299s, 752m, 700m. ¹H-NMR ((D₆)DMSO, 250 MHz): 9.02 (br. s, 1 NH); 7.85 (m, 1 fur. H); 7.36 (m, 5 arom. H); 7.14 (s, H–C(3)); 6.89 (dd, *J* = 3.5, 1.6, 1 fur. H); 6.65 (m, 1 fur. H); 5.08 (s, PhCH₂); 3.69 (s, MeO). MS: 301 (7, *M*⁺), 193 (10), 107 (14), 106 (20), 91 (100), 79 (18). Anal. calc. for C₁₆H₁₅NO₅ (301.298): C 63.78, H 5.02, N 4.65; found: C 63.70, H 5.10, N 4.57.

Methyl (Z)-2-[(Benzyloxy)carbonylamino]-3-(furan-3-yl)prop-2-enoate ((Z)-1b). From furan-3-carbaldehyde (**5b**; Aldrich; 1.8 ml, 21 mmol) in CH₂Cl₂ according to *Method A*: 5.74 g (91.5%) of (Z)-**1b**. M.p. 84.5°. IR (KBr): 3297m, 3063w, 1730s, 1699s, 1634s, 1555w, 1510s, 1271s, 752m, 700m. ¹H-NMR ((D₆)DMSO, 250 MHz): 9.02 (br. s, 1 NH); 8.10 (m, 1 fur. H); 7.73 (m, 1 fur. H); 7.39 (m, 5 arom. H); 7.31 (s, H–C(3)); 6.74 (m, 1 fur. H); 5.11 (s, PhCH₂); 3.70 (s, MeO). ¹³C-NMR ((D₆)DMSO, 400 MHz): 52.61 (q, MeO); 65.94 (t, PhCH₂); 110 (d, fur. CH); 119.94 (s, fur. C); 124.26 (s, C(2)); 125.44 (d, C(3)); 127.76, 127.97, 128.44 (3 d, 5 arom. C); 136.87 (s, 1 arom. C); 144.43 (d, fur. CH); 146.23 (d, fur. CH); 154.68 (s, COOCH₂Ph); 165.33 (s, COOMe). MS: 301 (6, *M*⁺), 91 (100). Anal. calc. for C₁₆H₁₅NO₅ (301.298): C 63.78, H 5.02, N 4.65; found: C 63.81, H 4.98, N 4.61.

Methyl (E)-2-[(Benzyloxy)carbonylamino]-3-(furan-3-yl)prop-2-enoate ((E)-1b). From the above reaction: 0.18 g (2.8%) of (E)-**1b**. M.p. 83.9°. IR (KBr): 3303m, 3063w, 1709s, 1641w, 1561m, 1525m, 1229s, 771w, 705w. ¹H-NMR ((D₆)DMSO, 250 MHz): 9.60 (br. s, 1 NH); 7.83 (m, 1 fur. H); 7.63 (m, 1 fur. H); 7.37 (m, 5 arom. H); 6.45 (m, 1 fur. H); 6.34 (s, H–C(3)); 5.08 (s, PhCH₂); 3.69 (s, MeO). MS: 301 (6, *M*⁺), 106 (10), 91 (100). Anal. calc. for C₁₆H₁₅NO₅ (301.298): C 63.78, H 5.02, N 4.65; found: C 63.49, H 4.99, N 4.58.

Methyl (Z)-2-[(Benzyloxy)carbonylamino]-3-(thiophen-2-yl)prop-2-enoate ((Z)-1c). From thiophene-2-carbaldehyde (**5c**; Fluka; 1.22 ml, 13.4 mmol) in CH₂Cl₂ according to *Method A*: 3.58 g (84%) of (Z)-**1c**. M.p. 113.5°. IR (KBr): 3296m, 3063w, 1732s, 1693s, 1629s, 1498s, 1229s, 767m, 713m. ¹H-NMR ((D₆)DMSO, 250 MHz): 8.95 (br. s, 1 NH); 7.81 (m, 1 thioph. H, H–C(3)); 7.57 (m, 1 thioph. H); 7.41 (m, 5 arom. H); 7.15 (dd, *J* = 5.1, 1.4, 1 thioph. H); 5.14 (s, PhCH₂); 3.72 (s, MeO). MS: 317 (6, *M*⁺), 182 (10), 107 (14), 122 (28), 92 (10), 91 (100), 79 (10), 65 (10). Anal. calc. for C₁₆H₁₅NO₄S (317.359): C 60.55, H 4.76, N 4.41, S 10.10; found: C 60.56, H 4.64, N 4.29, S 10.12.

Methyl (Z)-2-[(Benzyloxy)carbonylamino]-3-(thiophen-3-yl)prop-2-enoate ((Z)-1d). From thiophene-3-carbaldehyde (**5d**; Fluka; 1.91 ml, 21 mmol) in CH₂Cl₂ according to *Method A*: 6.34 g (95.2%) of (Z)-**1d**. M.p. 90°. IR (KBr): 3288m, 3091w, 1730s, 1690s, 1626s, 1522m, 1284s, 1223s, 786m, 697m. ¹H-NMR ((D₆)DMSO, 250 MHz): 9.11 (br. s, 1 NH); 7.96 (m, 1 thioph. H); 7.61 (dd, *J* = 7.9, 5.0, 1 thioph. H); 7.45 (m, 1 thioph. H); 7.40 (m, 5 arom. H); 5.10 (s, 2 aliph. H); 3.70 (s, MeO). ¹³C-NMR ((D₆)DMSO, 400 MHz): 52.06 (q, MeO); 65.77 (t, PhCH₂O); 123.61 (d, thioph. CH); 126.77, 127.55, 127.79, 127.86 (d, 5 arom. C, thioph. CH); 128.27 (d, thioph. CH); 130.23 (d, thioph. C); 134.75 (s, C(2)); 136.69 (s, arom. C); 154.59 (s, COOCH₂Ph); 165.52 (s, COOMe). MS: 317 (10, *M*⁺), 182 (10), 107 (14), 150 (12), 122 (18), 92 (10), 91 (100), 65 (10). Anal. calc. for C₁₆H₁₅NO₄S (317.359): C 60.55, H 4.76, N 4.41, S 10.10; found: C 60.48, H 4.79, N 4.34, S 10.09.

Methyl (Z)-2-[(Benzyloxy)carbonylamino]-3-(1H-pyrrol-2-yl)prop-2-enoate ((Z)-1e). From 1H-pyrrole-2-carbaldehyde (**5e**; Merck; 2.40 g, 25 mmol) in THF at –70° according to *Method A*: 4.20 g (56%) of (Z)-**1e**. M.p. 105.5°. IR (KBr): 3419m, 3031w, 1707s, 1690s, 1640s, 1515m, 1506w, 1248m, 713m, 692w. ¹H-NMR ((D₆)DMSO, 250 MHz): 11.30 (br. s, 1 NH); 8.72 (br. s, 1 NH); 7.38 (m, 5 arom. H, 1 pyr. H); 7.03 (s, H–C(3)); 6.62 (br. m, 1 pyr. H); 6.20 (br. m, 1 pyr. H); 5.09 (s, PhCH₂); 3.67 (s, MeO). MS: 300 (12, *M*⁺), 192 (10), 165 (30), 138 (10), 133 (14), 106 (26), 105 (40), 92 (10), 91 (100), 79 (24), 65 (12), 51 (18), 39 (10). Anal. calc. for C₁₆H₁₆N₂O₄ (300.314): C 63.99, H 5.37, N 9.33; found: C 63.82, H 5.50, N 9.26.

Methyl (Z)-2-[(Benzyloxy)carbonylamino]-3-{1-[(tert-butyloxy)carbonyl]-1H-pyrrol-2-yl}prop-2-enoate ((Z)-1f). From 1-[(tert-butyloxy)carbonyl]-1H-pyrrole-2-carbaldehyde (**5f**; 2.0 g, 10.3 mmol) in CH₂Cl₂ according to *Method A*: 2.46 g (60%) of (Z)-**1f**. M.p. 87.7°. IR (KBr): 3299m, 3143w, 1750s, 1727s, 1693s, 1630s, 1546w, 1522m, 1217m, 751m. ¹H-NMR ((D₆)DMSO, 250 MHz): 8.95 (br. s, 1 NH); 8.04 (s, H–C(3)); 7.46 (dd, *J* = 3.45, 1.68, 1 pyr. H); 7.35 (m, 5 arom. H); 6.87 (br. m, 1 pyr. H); 6.35 (br. m, 1 pyr. H); 5.07 (s, PhCH₂); 3.69 (s, MeO); 1.57 (s, *t*Bu). MS: 418.6 (65, [*M* + NH₄]⁺), 401.4 (100, [*M* + H]⁺). Anal. calc. for C₂₁H₂₄N₂O₆ (400.431): C 62.99, H 6.04, N 7.00; found: C 63.19, H 5.84, N 7.00.

(Z)-2-[(Benzyloxy)carbonylamino]-3-(furan-3-yl)prop-2-enoic Acid ((Z)-1'b). To a soln. of (Z)-**1b** (2 g, 6.63 mmol) in THF/H₂O 5:1 (180 ml) was added LiOH·H₂O (1.69 g, 39.8 mmol) under ice-bath cooling. The mixture was allowed to come to r.t. under vigorous stirring, then acidified with 1N aq. HCl, and extracted with AcOEt. The combined org. layers were washed with H₂O and brine, dried (Na₂SO₄), and evaporated. The residue was chromatographed (SiO₂, CHCl₃/MeOH/H₂O 3:1:0.1) to afford (Z)-**1'b** which was recrystallized from AcOEt/hexane: 1.33 g (71.8%). M.p. 134.8°. IR (KBr): 3287m (br.), 2592w (br.), 1686s, 1647s, 1555w, 1511m, 1248m, 741w, 687w. ¹H-NMR ((D₆)DMSO, 250 MHz): 12.67 (br. s, CO₂H); 8.75 (br. s, 1 NH); 8.05 (m, 1 fur. H); 7.72 (m, 1 fur. H); 7.38 (m, 5 arom. H); 7.28 (s, H–C(3)); 6.72 (m, 1 fur. H); 5.07 (s, PhCH₂). MS: 287 (3, *M*⁺), 108 (10), 107

(32), 91 (100), 79 (24), 77 (12), 65 (10), 51 (20). Anal. calc. for $C_{15}H_{13}NO_5$ (287.271): C 62.72, H 4.56, N 4.88; found: C 62.45, H 4.35, N 4.73.

tert-Butyl (Z)-2-[(Benzyloxy)carbonylamino]-3-(furan-2-yl)prop-2-enoate ((Z)-2a). From **5a** (1.25 ml, 14.5 mmol) in CH_2Cl_2 according to *Method B*: 4.33 g (86.5%) of (Z)-**2a**. M.p. 90°. IR (KBr): 3284m, 1702s, 1641m, 1585w, 1519s, 1252s, 752m, 699w. 1H -NMR ((D_6) DMSO, 250 MHz): 8.95 (br. s, 1 NH); 7.82 (m, 1 fur. H); 7.36 (m, 5 arom. H); 7.01 (s, H–C(3)); 6.84 (m, 1 fur. H); 6.62 (dd, $J = 3.42, 1.74$, 1 fur. H); 5.08 (s, $PhCH_2$); 1.40 (s, t-Bu). MS: 343 (4, M^+), 287 (14), 243 (10), 108 (10), 107 (16), 92 (10), 91 (100), 57 (14). Anal. calc. for $C_{19}H_{21}NO_5$ (343.379): C 66.46, H 6.16, N 4.08; found: C 66.53, H 6.08, N 4.10.

tert-Butyl (Z)-2-[(Benzyloxy)carbonylamino]-3-(furan-3-yl)prop-2-enoate ((Z)-2b). From **5b** (1.25 ml, 14.5 mmol) in CH_2Cl_2 according to *Method B*: 4.37 g (87.4%) of (Z)-**2b**. M.p. 65°. IR (KBr): 3357m, 1734s, 1692s, 1652s, 1508s, 1238s, 775m, 736m. 1H -NMR ((D_6) DMSO, 250 MHz): 8.95 (br. s, 1 NH); 8.05 (m, 1 fur. H); 7.71 (m, 1 fur. H); 7.37 (m, 5 arom. H); 7.15 (s, H–C(3)); 6.73 (m, 1 fur. H); 5.09 (s, $PhCH_2$); 1.40 (s, t-Bu). MS: 343 (< 1, M^+), 107 (10), 92 (10), 91 (100), 65 (10), 57 (20), 41 (12). Anal. calc. for $C_{19}H_{21}NO_5$ (343.379): C 66.46, H 6.16, N 4.08; found: C 66.23, H 6.07, N 3.84.

tert-Butyl (Z)-2-[(Benzyloxy)carbonylamino]-3-(thiophen-2-yl)prop-2-enoate ((Z)-2c). From **5c** (1.25 ml, 13.9 mmol) in CH_2Cl_2 according to *Method B*: 3.24 g (64.8%) of (Z)-**2c**. M.p. 99°. IR (KBr): 3275m, 1702s, 1633s, 1585w, 1517s, 1255s, 737m, 698m. 1H -NMR ((D_6) DMSO, 250 MHz): 8.81 (br. s, 1 NH); 7.74 (m, 1 thioph. H); 7.63 (s, H–C(3)); 7.51 (m, 1 thioph. H); 7.41 (m, 5 arom. H); 5.13 (s, $PhCH_2$); 1.42 (s, t-Bu). MS: 359 (1.5, M^+), 124 (14), 123 (12), 91 (100), 65 (10), 57 (24), 41 (14). Anal. calc. for $C_{19}H_{21}NO_4S$ (359.440): C 63.49, H 5.89, N 3.90, S 8.92; found: C 63.35, H 5.79, N 3.78, S 8.81.

tert-Butyl (Z)-2-[(Benzyloxy)carbonylamino]-3-(thiophen-3-yl)prop-2-enoate ((Z)-2d). From **5d** (0.204 ml, 2.23 mmol) in CH_2Cl_2 according to *Method B*: 0.65 g (81.2%) of (Z)-**2d**. M.p. 77.2°. IR (KBr): 3292m, 1701s, 1644m, 1585w, 1523s, 1251s, 738m, 697m. 1H -NMR ((D_6) DMSO, 250 MHz): 9.05 (br. s, 1 NH); 7.91 (m, 1 thioph. H); 7.59 (dd, $J = 5.0, 2.9$, 1 thioph. H); 7.38 (m, 5 arom. H, 1 thioph. H); 7.26 (s, H–C(3)); 5.10 (s, $PhCH_2$); 1.41 (s, t-Bu). MS: 359 (4, M^+), 303 (10), 123 (12), 92 (10), 91 (100), 57 (20), 41 (14). Anal. calc. for $C_{19}H_{21}NO_4S$ (359.440): C 63.49, H 5.89, N 3.90, S 8.92; found: C 63.56, H 5.85, N 3.90, S 8.72.

tert-Butyl (Z)-2-[(Benzyloxy)carbonylamino]-3-{1-[(tert-butoxy)carbonyl]pyrrol-2-yl}prop-2-enoate ((Z)-2f). From N-Boc-pyrrole-2-carbaldehyde (**5f**; 0.10 g, 0.513 mmol) in dioxane according to *Method B*: 0.073 g (32%) of (Z)-**2f**. 1H -NMR ((D_6) DMSO, 250 MHz): 8.91 (br. s, 1 NH); 7.84 (s, H–C(3)); 7.42 (m, 1 pyr. H); 7.35 (m, 5 arom. H); 6.83 (m, 1 pyr. H); 6.32 (m, 1 pyr. H); 5.08 (s, $PhCH_2$); 1.57 (s, t-Bu); 1.39 (s, t-Bu).

tert-Butyl (Z)-2-[(Benzyloxy)carbonylamino]-3-{1-[(4-methylphenyl)sulfonyl]-1H-pyrrol-2-yl}prop-2-enoate ((Z)-2g). From 1-tosyl-1H-pyrrole-2-carbaldehyde (**5g**; 5.0 g, 49.16 mmol) in DME according to *Method B*: 5.15 g (64.9%) of (Z)-**2g**. M.p. 111.9°. IR (KBr): 3238m, 1717s, 1634m, 1595w, 1496w, 1336m, 1251m, 1156s, 732m, 701m. 1H -NMR ((D_6) DMSO, 250 MHz): 8.95 (br. s, 1 NH); 7.76 (m, 2 arom. H); 7.64 (m, 1 pyr. H, H–C(3)); 7.46 (m, 2 arom. H); 7.33 (m, 5 arom. H); 6.86 (m, 1 pyr. H); 5.04 (s, $PhCH_2$); 2.36 (s, MeO); 1.44 (s, t-Bu). MS: 496 (4, M^+), 440 (10), 332 (10), 261 (14), 177 (12), 155 (16), 106 (10), 105 (36), 92 (10), 91 (100), 65 (14), 57 (20), 41 (14). Anal. calc. for $C_{26}H_{28}N_2O_6$ (496.578): C 62.89, H 5.68, N 5.64, S 6.46; found: C 62.90, H 5.70, N 5.55, S 6.58.

Methyl (S)-2-[(Benzyloxy)carbonylamino]-3-(furan-2-yl)propanoate ((S)-3a). From (Z)-**1a** (1.5 g, 4.98 mmol) in MeOH (15 ml), using $[Rh(cod)(IIIb)]BF_4$ according to *Method C*: 1.25 g (82.6%) of (S)-**3a**. Oil. $[\alpha]_D^{25} = +49.1$ ($c = 1.00$, $CHCl_3$); ee 98.8%. IR (film): 3341m (br.), 1724s, 1589w, 1509s, 1260m, 1214m, 738m, 698m. 1H -NMR ((D_6) DMSO, 250 MHz): 7.86 (d, $J = 8.0$, 1 NH); 7.53 (m, 1 fur. H); 7.34 (m, 5 arom. H); 6.35 (dd, $J = 3.0, 1.9$, 1 fur. H); 6.16 (m, 1 fur. H); 5.01 (s, $PhCH_2$); 4.31 (m, 1 aliph. H); 3.62 (s, MeO); 3.01 (m, 2 H–C(3)). MS: 303 (< 1, M^+), 108 (10), 92 (10), 91 (100), 81 (34), 65 (12), 53 (11). Anal. calc. for $C_{16}H_{17}NO_5$ (303.314): C 63.36, H 5.65, N 4.62; found: C 63.57, H 5.71, N 4.61.

Methyl (R)-2-[(Benzyloxy)carbonylamino]-3-(furan-2-yl)propanoate ((R)-3a). From (Z)-**1a** (1.5 g, 4.98 mmol) in MeOH (15 ml), using $[Rh(cod)(IIIa)]BF_4$ according to *Method C*: 1.50 g (99%) of (R)-**3a**. Oil. $[\alpha]_D^{25} = -50.2$ ($c = 1.00$, $CHCl_3$); ee 98.4%. IR, 1H -NMR, MS: identical to those of (S)-**3a**. Anal. calc. for $C_{16}H_{17}NO_5$ (303.314): C 63.36, H 5.65, N 4.62; found: C 63.47, H 5.66, N 4.58.

Methyl (S)-2-[(Benzyloxy)carbonylamino]-3-(furan-3-yl)propanoate ((S)-3b). From (Z)-**1b** (0.20 g, 0.66 mmol) in MeOH (5 ml), using $[Rh(cod)(IIIb)]BF_4$ according to *Method C*: 0.195 g (97%) of (S)-**3b**. Oil. $[\alpha]_D^{25} = +35.1$ ($c = 0.4$, $CHCl_3$); ee 97.5%. IR (film): 3341m (br.), 1742s, 1582w, 1519s, 1213m, 1179m, 738w, 698w. 1H -NMR ((D_6) DMSO, 250 MHz): 7.82 (d, $J = 7.9$, 1 NH); 7.55 (m, 1 fur. H); 7.46 (m, 1 fur. H); 7.32 (m, 5 arom. H); 6.40 (m, 1 fur. H); 5.01 (s, 2 aliph. H); 4.18 (m, 1 aliph. H); 3.63 (s, MeO); 2.84 (dd, $J = 14.5, 5.1$, 1 aliph. H); 2.70 (dd, $J = 14.5, 9.7$, 1 aliph. H). MS: 303 (< 1, M^+), 152 (30), 92 (10), 91 (100), 81 (24), 65 (12), 53 (10). Anal. calc. for $C_{16}H_{17}NO_5$ (303.314): C 63.36, H 5.65, N 4.62; found: C 63.43, H 5.68, N 4.63.

Methyl (R)-2-[(Benzyloxy)carbonylamino]-3-(furan-3-yl)propanoate ((R)-3b). From (Z)-1b (0.20, 0.66 mmol) in MeOH (5 ml), using [Rh(cod)(IIIa)]BF₄, according to *Method C*: 0.193 g (96%) of (R)-3b. Oil. $[\alpha]_D = -32.1$ (*c* = 0.5, CHCl₃); ee 97.9%. IR, ¹H-NMR, MS: identical to those of (S)-3b. Anal. calc. for C₁₆H₁₇NO₅ (303.314): C 63.36, H 5.65, N 4.62; found: C 63.19, H 5.74, N 4.64.

Methyl (S)-2-[(Benzyloxy)carbonylamino]-3-(thiophen-2-yl)propanoate ((S)-3c). From (Z)-1c (0.20 g, 0.63 mmol) in MeOH (5 ml), using [Rh(cod)(IIIb)]BF₄, according to *Method C*: 0.20 g (99%) of (S)-3c. Oil. $[\alpha]_D = +55.6$ (*c* = 0.5, CHCl₃); ee 98.1%. IR (film): 3338m (br.), 1735s, 1722s, 1587w, 1516s, 1275s, 1212s, 739w, 698m. ¹H-NMR ((D₆)DMSO, 250 MHz): 7.90 (*d*, *J* = 8.2, 1 NH); 7.33 (*m*, 1 thioph. H, 5 arom. H); 6.94 (*m*, 2 thioph. H); 5.02 (*s*, PhCH₂); 4.25 (*m*, 1 aliph. H); 3.64 (*s*, MeO); 3.28 (*dd*, *J* = 14.9, 4.8, 1 aliph. H); 3.11 (*dd*, *J* = 14.9, 9.8, 1 aliph. H). MS: 319 (< 1, *M*⁺), 196 (10), 169 (10), 168 (70), 97 (58), 91 (100), 65 (10). Anal. calc. for C₁₆H₁₇NO₄S (319.375): C 60.17, H 5.37, N 4.39, S 10.04; found: C 60.32, H 5.51, N 4.31, S 9.75.

Methyl (R)-2-[(Benzyloxy)carbonylamino]-3-(thiophen-2-yl)propanoate ((R)-3c). From (Z)-1c (0.20 g, 0.63 mmol) in MeOH (5 ml), using [Rh(cod)(IIIa)]BF₄, according to *Method C*: 0.188 g (93.5%) of (R)-3c. Oil. $[\alpha]_D = -55.4$ (*c* = 0.5, CHCl₃); ee 98.0%. IR, ¹H-NMR, MS: identical to those of (S)-3c. Anal. calc. for C₁₆H₁₇NO₄S (319.375): C 60.17, H 5.37, N 4.39, S 10.04; found: C 60.17, H 5.47, N 4.37, S 9.74.

Methyl (S)-2-[(Benzyloxy)carbonylamino]-3-(thiophen-3-yl)propanoate ((S)-3d). From (Z)-1d (0.20 g, 0.63 mmol) in MeOH (5 ml), using [Rh(cod)(IIIb)]BF₄, according to *Method C*: 0.199 g (99%) of (S)-3d. Oil. $[\alpha]_D = +46.1$ (*c* = 0.5, CHCl₃); ee 96.5%. IR (film): 3342m (br.), 1735s, 1723s, 1583w, 1520s, 1261s, 1213s, 773w, 698m. ¹H-NMR ((D₆)DMSO, 250 MHz): 7.84 (*d*, *J* = 7.0, 1 NH); 7.44 (*dd*, *J* = 4.9, 2.9, 1 thioph. H); 7.31 (*m*, 5 arom. H); 7.23 (*m*, 1 thioph. H); 7.03 (*m*, 1 thioph. H); 5.00 (*s*, PhCH₂); 4.25 (*m*, 1 aliph. H); 3.62 (*s*, MeO); 3.05 (*dd*, *J* = 14.9, 5.6, 1 aliph. H); 2.91 (*dd*, *J* = 14.9, 9.3, 1 aliph. H). MS: 319 (< 1, *M*⁺), 168 (34), 97 (38), 91 (100), 65 (10). Anal. calc. for C₁₆H₁₇NO₄S (319.375): C 60.17, H 5.37, N 4.39, S 10.04; found: C 60.17, H 5.36, N 4.39, S 9.77.

Methyl (R)-2-[(Benzyloxy)carbonylamino]-3-(thiophen-3-yl)propanoate ((R)-3d). From (Z)-1d (0.20 g, 0.63 mmol) in MeOH (5 ml), using [Rh(cod)(IIIa)]BF₄, according to *Method C*: 0.197 g (98%) of (R)-3d. Oil. $[\alpha]_D = -45.0$ (*c* = 0.5, CHCl₃); ee 96.5%. IR, ¹H-NMR, MS: identical to those of (S)-3d. Anal. calc. for C₁₆H₁₇NO₄S (319.375): C 60.17, H 5.37, N 4.39, S 10.04; found: C 60.08, H 5.37, N 4.36, S 9.85.

Methyl (S)-2-[(Benzyloxy)carbonylamino]-3-(1H-pyrrol-2-yl)propanoate ((S)-3e). From (Z)-1e (0.20, 0.67 mmol) in MeOH (5 ml), using [Rh(cod)(IIIb)]BF₄, according to *Method C*: 0.125 g (62.2%) of (S)-3e. Oil. $[\alpha]_D = +27.4$ (*c* = 0.5, CHCl₃); ee 94.5%. IR (film): 3370m (br.), 1714s, 1582w, 1515s, 1256s, 1216s, 726w, 699m. ¹H-NMR ((D₆)DMSO, 250 MHz): 10.56 (br. *s*, 1 NH); 7.69 (br. *d*, *J* = 8.7, 1 NH); 7.33 (*m*, 5 arom. H); 6.60 (*m*, 1 pyr. H); 5.86 (*m*, 1 pyr. H); 5.78 (*m*, 1 pyr. H); 5.00 (*s*, 2 aliph. H); 4.26 (*m*, 1 aliph. H); 3.60 (*s*, MeO); 2.96 (*dd*, *J* = 14.9, 5.0, 1 aliph. H); 2.84 (*dd*, *J* = 14.9, 10.0, 1 aliph. H). MS: 302 (13, *M*⁺), 151 (14), 91 (26), 80 (100). Anal. calc. for C₁₆H₁₈N₂O₄ (302.330): C 63.56, H 6.00, N 9.27; found: C 63.24, H 6.15, N 9.00.

Methyl (S)-2-[(Benzyloxy)carbonylamino]-3-{1-[(tert-butyloxy)carbonyl]-1H-pyrrol-2-yl}propanoate ((S)-3f). From (Z)-1f (0.20 g, 0.50 mmol) in MeOH (5 ml), using [Rh(cod)(IIIb)]BF₄, according to *Method C*: 0.196 g (97.4%) of (S)-3f. Oil. $[\alpha]_D = -27.7$ (*c* = 1.00, EtOH); ee 97.2%. IR (film): 3367m (br.), 1739s, 1715s, 1582w, 1521s, 1248s, 1213s, 730w, 697m. ¹H-NMR ((D₆)DMSO, 250 MHz): 7.76 (br. *d*, *J* = 8.2, 1 NH); 7.32 (*m*, 5 arom. H); 7.18 (*dd*, *J* = 3.3, 1.8, 1 pyr. H); 6.09 (*m*, 1 pyr. H); 6.01 (*m*, 1 pyr. H); 4.99 (*s*, PhCH₂); 4.42 (*m*, 1 aliph. H); 3.58 (*s*, MeO); 3.28 (*dd*, *J* = 14.9, 5.8, 1 aliph. H); 3.07 (*dd*, *J* = 14.9, 9.7, 1 aliph. H); 1.54 (*s*, *t*Bu). MS: 402 (< 1, *M*⁺), 151 (18), 97 (10), 91 (40), 83 (16), 80 (100), 71 (14), 69 (12), 57 (70), 55 (24), 44 (12), 43 (56), 41 (34), 32 (16). Anal. calc. for C₂₁H₂₆N₂O₆ (402.447): C 62.67, H 6.51, N 6.96; found: C 62.44, H 6.63, N 6.77.

tert-Butyl (S)-2-[(Benzyloxy)carbonylamino]-3-(furan-2-yl)propanoate ((S)-4a). From (Z)-2a (1.6 g, 4.6 mmol) in MeOH (20 ml), using [Rh(cod)(IIIb)]BF₄, according to *Method C*: 1.57 g (97.5%) of (S)-4a. Oil. $[\alpha]_D = +41.2$ (*c* = 1.00, CHCl₃); ee 99.5%. IR (film): 3340m (br.), 1721s, 1598w, 1505s, 1221s, 1156s, 736m, 698m. ¹H-NMR ((D₆)DMSO, 250 MHz): 7.71 (*d*, *J* = 8.0, 1 NH); 7.54 (*m*, 1 fur. H); 7.33 (*m*, 5 arom. H); 6.35 (*dd*, *J* = 3.0, 1.7, 1 fur. H); 6.16 (*m*, 1 fur. H); 5.02 (*s*, PhCH₂); 4.17 (*m*, 1 aliph. H); 2.94 (*m*, 2 aliph. H); 1.34 (*s*, *t*Bu). MS: 345 (< 1, *M*⁺), 138 (16), 92 (10), 91 (100), 65 (14), 57 (40), 53 (10), 41 (16), 39 (12). Anal. calc. for C₁₉H₂₃NO₅ (345.395): C 66.07, H 6.71, N 4.06; found: C 66.08, H 6.78, N 4.08.

tert-Butyl (R)-2-[(Benzyloxy)carbonylamino]-3-(furan-2-yl)propanoate ((R)-4a). From (Z)-2a (2.0 g, 5.8 mmol) in MeOH (20 ml), using [Rh(cod)(IIIa)]BF₄, according to *Method C*: 1.61 g (80%) of (R)-4a. Oil. $[\alpha]_D = -41.2$ (*c* = 1.00, CHCl₃); ee 99.6%. IR, ¹H-NMR, MS: identical to those of (S)-4a. Anal. calc. for C₁₉H₂₃NO₅ (345.395): C 66.07, H 6.71, N 4.06; found: C 66.03, H 6.74, N 4.03.

tert-Butyl (S)-2-[(Benzyloxy)carbonylamino]-3-(furan-3-yl)propanoate ((S)-4b). From (Z)-2b (2.0 g, 5.8 mmol) in MeOH (20 ml), using [Rh(cod)(IIIb)]BF₄, according to *Method C*: 1.81 g (90%) of (S)-4b. Oil. $[\alpha]_D = +29.2$ (*c* = 1.00, CHCl₃); ee 98.9%. IR (film): 3402m (br.), 1741s, 1700s, 1588w, 1521s, 1251s, 1150s,

754m, 698m. ¹H-NMR ((D₆)DMSO, 250 MHz): 7.69 (*d*, *J* = 7.9, 1 NH); 7.55 (*m*, 1 fur. H); 7.45 (*m*, 1 fur. H); 7.33 (*m*, 5 arom. H); 6.42 (*m*, 1 fur. H); 5.02 (*s*, PhCH₂); 4.04 (*m*, 1 aliph. H); 2.71 (*m*, 2 aliph. H); 1.35 (*s*, *t*Bu). MS: 345 (< 1, *M*⁺), 138 (14), 92 (10), 91 (100), 81 (10), 65 (10), 57 (26), 41 (10). Anal. calc. for C₁₉H₂₃NO₅ (345.395): C 66.07, H 6.71, N 4.06; found: C 65.79, H 6.60, N 3.93.

tert-Butyl (R)-2-[(Benzyloxy)carbonylamino]-3-(furan-3-yl)propanoate ((R)-4b). From (Z)-2b (2.0 g, 5.8 mmol) in MeOH (20 ml), using [Rh(cod)(IIIa)]BF₄ according to Method C: 1.84 g (91.5%) of (R)-4b. Oil. [α]_D = −30.9 (*c* = 1.00, CHCl₃); ee 98.4%. IR, ¹H-NMR, MS: identical to those of (S)-4b. Anal. calc. for C₁₉H₂₃NO₅ (345.395): C 66.07, H 6.71, N 4.06; found: C 65.90, H 6.69, N 3.85.

tert-Butyl (S)-2-[(Benzyloxy)carbonylamino]-3-(thiophen-2-yl)propanoate ((S)-4c). From (Z)-2c (2.0 g, 5.56 mmol) in MeOH (20 ml), using [Rh(cod)(IIIb)]BF₄ according to Method C: 1.94 g (96.5%) of (S)-4c. Oil. [α]_D = +43.6 (*c* = 1.00, CHCl₃); ee 99.0%. IR (film): 3346m (br.), 1724s, 1585w, 1504m, 1244s, 1220s, 750w, 697m. ¹H-NMR ((D₆)DMSO, 250 MHz): 7.77 (*d*, *J* = 8.1, 1 NH); 7.34 (*m*, 1 thioph. H, 5 arom. H); 6.93 (*m*, 2 thioph. H); 5.02 (*s*, PhCH₂); 4.10 (*m*, 1 aliph. H); 3.24 (*dd*, *J* = 14.8, 5.4, 1 aliph. H); 3.07 (*dd*, *J* = 14.8, 9.3, 1 aliph. H); 1.35 (*s*, *t*Bu). MS: 361 (< 1, *M*⁺), 154 (12), 97 (24), 91 (100), 65 (10), 57 (34), 41 (14), 39 (10). Anal. calc. for C₁₉H₂₃NO₄S (361.456): C 63.14, H 6.41, N 3.88, S 8.87; found: C 63.11, H 6.46, N 3.88, S 8.83.

tert-Butyl (R)-2-[(Benzyloxy)carbonylamino]-3-(thiophen-2-yl)propanoate ((R)-4c). From (Z)-2c (2.9 g, 8.07 mmol) in MeOH (20 ml), using [Rh(cod)(IIIa)]BF₄ according to Method C: 2.88 g (98.5%) of (R)-4c. Oil. [α]_D = −43.5 (*c* = 1.00, CHCl₃); ee 99.1%. IR, ¹H-NMR, MS: identical to those of (S)-4c. Anal. calc. for C₁₉H₂₃NO₄S (361.456): C 63.14, H 6.41, N 3.88, S 8.87; found: C 63.22, H 6.43, N 3.68, S 8.84.

tert-Butyl (S)-2-[(Benzyloxy)carbonylamino]-3-(thiophen-3-yl)propanoate ((S)-4d). From (Z)-2d (0.63 g, 1.75 mmol) in MeOH (15 ml), using [Rh(cod)(IIIb)]BF₄ according to Method C: 0.631 g (99.5%) of (S)-4d. M.p. 83.5°. [α]_D = +40.2 (*c* = 0.9, CHCl₃); ee 98.4%. IR (KBr): 3395m (br.), 1740s, 1698s, 1583w, 1517s, 1267m, 1217m, 752w, 698m. ¹H-NMR ((D₆)DMSO, 250 MHz): 7.72 (*d*, *J* = 7.9, 1 NH); 7.44 (*dd*, *J* = 4.9, 2.9, 1 thioph. H); 7.33 (*m*, 5 arom. H); 7.22 (*m*, 1 thioph. H); 7.04 (*m*, 1 thioph. H); 5.00 (*s*, 2 aliph. H); 4.14 (*m*, 1 aliph. H); 2.97 (*dd*, *J* = 14.9, 5.8, 1 aliph. H); 2.88 (*dd*, *J* = 14.9, 9.3, 1 aliph. H); 1.33 (*s*, *t*Bu). MS: 361 (< 1, *M*⁺), 154 (12), 97 (18), 91 (100), 65 (12), 57 (36), 41 (14), 39 (10). Anal. calc. for C₁₉H₂₃NO₄S (361.456): C 63.14, H 6.41, N 3.88, S 8.87; found: C 62.95, H 6.51, N 3.73, S 9.15.

tert-Butyl (R)-2-[(Benzyloxy)carbonylamino]-3-(thiophen-3-yl)propanoate ((R)-4d). From (Z)-2d (2.2 g, 6.12 mmol) in MeOH (20 ml), using [Rh(cod)(IIIa)]BF₄ according to Method C: 2.2 g (99.5%) of (R)-4d. M.p. 83°. [α]_D = −39.5 (*c* = 1.00, CHCl₃); ee 98.4%. IR, ¹H-NMR, MS: identical to those of (S)-4d. Anal. calc. for C₁₉H₂₃NO₄S (361.456): C 63.14, H 6.41, N 3.88, S 8.87; found: C 62.94, H 6.45, N 3.73.

tert-Butyl (S)-2-[(Benzyloxy)carbonylamino]-3-{1-[(4-methylphenyl)sulfonyl]-1H-pyrrol-2-yl}propanoate ((S)-4g). From (Z)-2g (2.0 g, 4.03 mmol) in MeOH (20 ml), using [Rh(cod)(IIIb)]BF₄ according to Method C: 1.8 g (90.5%) of (S)-4g. Oil. [α]_D = +12.2 (*c* = 0.6, CHCl₃); ee 99.1%. IR (film): 3392m (br.), 1724s, 1596w, 1518m, 1367s, 1227s, 1175s, 720m, 672m. ¹H-NMR ((D₆)DMSO, 250 MHz): 7.74 (*d*, *J* = 8.3, 2 arom. H); 7.71 (br. *d*, *J* = 7.9, 1 NH); 7.46 (*d*, *J* = 8.3, 2 arom. H); 7.33 (*m*, 5 arom. H, 1 pyr. H); 6.25 (*m*, 1 pyr. H); 6.10 (*m*, 1 pyr. H); 5.00 (*s*, PhCH₂); 4.20 (*m*, 1 aliph. H); 3.08 (*dd*, *J* = 15.5, 5.3, 1 aliph. H); 2.99 (*dd*, *J* = 15.5, 9.6, 1 aliph. H); 2.37 (*s*, arom. Me); 1.34 (*s*, *t*Bu). MS: 498 (< 1, *M*⁺), 234 (30), 92 (10), 91 (100), 80 (14), 57 (26), 41 (12), 39 (10). Anal. calc. for C₂₆H₃₀N₂O₆S (498.594): C 62.63, H 6.07, N 5.62, S 6.43; found: C 62.73, H 6.15, N 5.34, S 6.32.

tert-Butyl (R)-2-[(Benzyloxy)carbonylamino]-3-{1-[(4-methylphenyl)sulfonyl]-1H-pyrrol-2-yl}propanoate ((R)-4g). From (Z)-2g (1.03 g, 2.67 mmol) in MeOH (15 ml), using [Rh(cod)(IIIa)]BF₄ according to Method C: 0.98 g (95.2%) of (R)-4g. Oil. [α]_D = −10.8 (*c* = 0.5, CHCl₃); ee 98.5%. IR, ¹H-NMR, MS: identical to those of (S)-4g. Anal. calc. for C₂₆H₃₀N₂O₆S (498.594): C 62.63, H 6.07, N 5.62, S 6.43; found: C 62.45, H 6.15, N 5.41, S 6.41.

1-[(tert-Butyloxy)carbonyl]-1H-pyrrole-2-carbaldehyde (5f). To a stirred soln. of 5e (1.0 g, 1.05 mmol) in CH₂Cl₂ (100 ml) were added under Ar, at r.t., a catalytic amount of DMAP, (i-Pr)₂EtN (Fluka; 2.34 ml, 13.7 mmol), and di(tert-butyl) dicarbonate (Fluka; 2.98 g, 13.7 mmol). The mixture was quenched with 1N aq. KHSO₄, extracted with CHCl₃, the combined org. layer washed with brine (10 ml), dried (Na₂SO₄), and evaporated, and the residue chromatographed (SiO₂, AcOEt/hexane/CHCl₃ 1:3:1): 5f (1.88 g, 91.7%). Yellow oil. IR (film): 3175w, 1749s, 1668s, 1544m, 1166s, 1126s. ¹H-NMR (CDCl₃, 250 MHz): 10.32 (*s*, CHO); 7.44 (*dd*, *J* = 3.1, 1.7, 1 pyr. H); 7.18 (*dd*, *J* = 3.7, 1.7, 1 pyr. H); 6.28 (*m*, 1 pyr. H); 1.64 (*s*, *t*Bu). MS: 195 (< 1, *M*⁺), 122 (10), 95 (26), 94 (14), 57 (100), 41 (36), 39 (18), 29 (22). Anal. calc. for C₁₀H₁₃NO₃ (195.218): C 61.53, H 6.71, N 7.18; found: C 61.59, H 6.91, N 7.32.

1-[(4-Methylphenyl)sulfonyl]-1H-pyrrole-2-carbaldehyde (5g). As described for 5f, with 5e (5.0 g, 52 mmol), CHCl₂ (200 ml), cat. DMAP, (i-Pr)₂EtN (11.7 ml, 68 mmol), and TsCl (Fluka; 13.02 g, 68 mmol): 5g (12.64 g,

96.5%). Pale brown powder. M.p. 94.6°. IR (KBr): 3124w, 1666s, 1594m, 1530m, 1489m, 1365s, 1175s, 1153s, 810w, 777m, 752m. ¹H-NMR ((D₆)DMSO, 250 MHz): 9.87 (s, CHO); 7.94 (d, *J* = 8.4, 2 arom. H); 7.88 (dd, *J* = 3.1, 1.7, 1 pyr. H); 7.49 (d, *J* = 8.4, 2 arom. H); 7.29 (dd, *J* = 3.7, 1.7, 1 pyr. H); 6.57 (m, 1 pyr. H); 2.39 (s, arom. Me). MS: 249 (< 1, *M*⁺), 185 (16), 155 (16), 94 (16), 92 (16), 91 (100), 65 (38), 63 (10), 39 (36), 38 (10). Anal. calc. for C₁₂H₁₁NO₃S (249.284): C 57.82, H 4.45, N 5.62, S 12.86; found: C 57.64, H 4.48, N 5.42, S 12.94.

(*S*)-2-[(*Benzyl*oxy)carbonylamino]-3-(furan-3-yl)propanoic Acid ((*S*)-7b). From (*S*)-4b (1.10 g, 3.18 mmol) in CH₂Cl₂/H₂O/CF₃COOH (36 ml) according to *Method E*: 0.731 g (79.5%) of (*S*)-7b. White powder. M.p. 78°. [α]_D = +39.5 (*c* = 1.00, CHCl₃); ee 99.1%. IR (KBr): 3339m (br.), 1722s, 1701s, 1665s, 1585w, 1527s, 1265s, 1236s, 736w, 698w. ¹H-NMR ((D₆)DMSO, 250 MHz): 12.73 (br. s, CO₂H); 7.63 (d, *J* = 8.2, 1 NH); 7.55 (m, 1 fur. H); 7.45 (m, 1 fur. H); 7.33 (m, 5 arom. H); 6.40 (m, 1 fur. H); 5.00 (s, PhCH₂); 4.11 (m, 1 aliph. H); 2.87 (dd, *J* = 14.9, 5.0, 1 aliph. H); 2.70 (dd, *J* = 14.9, 10.0, 1 aliph. H). MS: 289 (< 1, *M*⁺), 154 (10), 138 (18), 108 (22), 107 (14), 92 (10), 91 (100), 82 (10), 81 (94), 79 (28), 65 (14), 53 (26), 51 (10), 39 (12). Anal. calc. for C₁₅H₁₅NO₅ (289.287): C 62.28, H 5.23, N 4.84; found: C 62.10, H 5.38, N 4.77.

(*R*)-2-[(*Benzyl*oxy)carbonylamino]-3-(furan-3-yl)propanoic Acid ((*R*)-7b). From (*R*)-4b (1.10 g, 3.18 mmol) in CH₂Cl₂/H₂O/CF₃COOH (36 ml) according to *Method E*: 0.759 g (82.5%) of (*R*)-7b. White powder. M.p. 78°. [α]_D = -37.5 (*c* = 1.00, CHCl₃); ee 98.6%. IR, ¹H-NMR, MS: identical to those of (*S*)-7b. Anal. calc. for C₁₅H₁₅NO₅ (289.287): C 62.28, H 5.23, N 4.84; found: C 62.35, H 5.55, N 4.79.

(*S*)-2-[(*Benzyl*oxy)carbonylamino]-3-(thiophen-2-yl)propanoic Acid [26] ((*S*)-7c). From (*S*)-4c (0.617 g, 1.70 mmol) in CH₂Cl₂/H₂O/CF₃COOH (21.7 ml) according to *Method E*: 0.454 g (87.2%) of (*S*)-7c. White powder. M.p. 86.5°. [α]_D = +49.0 (*c* = 1.00, CHCl₃); ee 99.4%. IR (KBr): 3330m (br.), 1715s, 1699s, 1669s, 1583w, 1531s, 1225m, 735w, 684w. ¹H-NMR ((D₆)DMSO, 250 MHz): 12.86 (br. s, CO₂H); 7.71 (d, *J* = 8.1, 1 NH); 7.33 (m, 5 arom. H, 1 thioph. H); 6.92 (m, 2 thioph. H); 5.01 (s, PhCH₂); 4.17 (m, 1 aliph. H); 3.30 (dd, *J* = 14.8, 5.4, 1 aliph. H); 3.09 (dd, *J* = 14.8, 9.3, 1 aliph. H). MS: 303.9 (100, [*M* - H]⁺). Anal. calc. for C₁₅H₁₅NO₄S (305.348): C 59.00, H 4.95, N 4.59, S 10.50; found: C 59.18, H 5.25, N 4.45, S 10.55.

(*R*)-2-[(*Benzyl*oxy)carbonylamino]-3-(thiophen-2-yl)propanoic Acid [26] ((*R*)-7c). From (*R*)-4c (1.40 g, 3.87 mmol) in CH₂Cl₂/H₂O/CF₃COOH (50.5 ml) according to *Method E*: 0.988 g (83.7%) of (*R*)-7c. White powder. M.p. 86.5°. [α]_D = -49.3 (*c* = 1.00, CHCl₃); ee 98.9%. IR, ¹H-NMR, MS: identical to those of (*S*)-7c. Anal. calc. for C₁₅H₁₅NO₄S (305.348): C 59.00, H 4.95, N 4.59, S 10.50; found: C 59.11, H 5.20, N 4.46, S 10.48.

(*S*)-2-[(*Benzyl*oxy)carbonylamino]-3-(thiophen-3-yl)propanoic Acid [26] ((*S*)-7d). From (*S*)-4d (0.87 g, 2.4 mmol) in CH₂Cl₂/H₂O/CF₃COOH (36 ml) according to *Method E*: 0.662 g (90.5%) of (*S*)-7d. White powder. M.p. 90°. [α]_D = +54.2 (*c* = 1.00, CHCl₃); ee 99.8%. IR (KBr): 3324m (br.), 1715s, 1698s, 1668s, 1585w, 1531s, 1263m, 1223m, 784w, 696w. ¹H-NMR ((D₆)DMSO, 250 MHz): 12.75 (br. s, CO₂H); 7.65 (d, *J* = 7.9, 1 NH); 7.45 (dd, *J* = 4.9, 3.0, 1 thioph. H); 7.30 (m, 5 arom. H); 7.24 (m, 1 thioph. H); 7.03 (m, 1 thioph. H); 4.99 (s, PhCH₂); 4.17 (m, 1 aliph. H); 3.07 (dd, *J* = 14.9, 5.8, 1 aliph. H); 2.88 (dd, *J* = 14.9, 9.3, 1 aliph. H). MS: 323.3 (100, [*M* + NH₄]⁺). Anal. calc. for C₁₅H₁₅NO₄S (305.348): C 59.00, H 4.95, N 4.59, S 10.50; found: C 59.05, H 4.69, N 4.35, S 10.58.

(*R*)-2-[(*Benzyl*oxy)carbonylamino]-3-(thiophen-3-yl)propanoic Acid [26] ((*R*)-7d). From (*R*)-4d (1.07 g, 2.96 mmol) in CH₂Cl₂/H₂O/CF₃COOH (36 ml) according to *Method E*: 0.804 g (89%) of (*R*)-7d. White powder. M.p. 89.5°. [α]_D = -51.3 (*c* = 1.00, CHCl₃); ee 99.5%. IR, ¹H-NMR, MS: identical to those of (*S*)-7d. Anal. calc. for C₁₅H₁₅NO₄S (305.348): C 59.00, H 4.95, N 4.59, S 10.50; found: C 59.00, H 4.78, N 4.39, S 10.60.

(*S*)-2-[(*Benzyl*oxy)carbonylamino]-3-{1-[(4-methylphenyl)sulfonyl]-1H-pyrrol-2-yl}propanoic Acid [26] ((*S*)-7g). From (*S*)-4g (0.90 g, 1.8 mmol) in CH₂Cl₂/H₂O/CF₃COOH (36 ml) according to *Method E*: 0.613 g (76.8%) of (*S*)-7g. White powder. M.p. 84.5°. [α]_D = -6.2 (*c* = 1.00, CHCl₃); ee 99.0%. IR (KBr): 3410m (br.), 1722s, 1590w, 1527s, 1366s, 1215m, 1175m, 805w, 678w. ¹H-NMR ((D₆)DMSO, 250 MHz): 12.77 (br. s, CO₂H); 7.72 (d, *J* = 8.3, 2 arom. H); 7.64 (br. s, 1 NH); 7.43 (d, *J* = 8.3, 2 arom. H); 7.32 (m, 5 arom. H, 1 pyr. H); 6.24 (m, 1 pyr. H); 6.10 (m, 1 pyr. H); 4.99 (s, PhCH₂); 4.26 (m, 1 aliph. H); 3.22 (dd, *J* = 15.5, 5.3, 1 aliph. H); 2.96 (dd, *J* = 15.5, 9.5, 1 aliph. H). MS: 460.4 (100, [*M* + NH₄]⁺). Anal. calc. for C₂₂H₂₂N₂O₆S (442.486): C 59.72, H 5.01, N 6.33, S 7.25; found: C 59.47, H 4.82, N 6.14, S 7.27.

(*R*)-2-[(*Benzyl*oxy)carbonylamino]-3-{1-[(4-methylphenyl)sulfonyl]-1H-pyrrol-2-yl}propanoic Acid ((*R*)-7g). From (*R*)-4g (0.87 g, 1.74 mmol) in CH₂Cl₂/H₂O/CF₃COOH (35 ml) according to *Method E*: 0.635 g (82.6%) of (*R*)-7g. White powder. M.p. 84.5°. [α]_D = +6.7 (*c* = 1.00, CHCl₃); ee 99.0%. IR, ¹H-NMR, MS: identical to those of (*S*)-7g. Anal. calc. for C₂₂H₂₂N₂O₆S (442.486): C 59.72, H 5.01, N 6.33, S 7.25; found: C 59.63, H 4.88, N 6.14, S 7.25.

Dicyclohexylammonium (*S*)-2-[(*Benzyl*oxy)carbonylamino]-3-(furan-2-yl)propanoate ((*S*)-8a). From (*S*)-4a (1.55 g, 4.48 mmol) in CH₂Cl₂/H₂O/CF₃COOH (50 ml) according to *Method E*: 1.55 g (100%) of oily (*S*)-7a [26];

ee 99.5%. Further conversion using dicyclohexylamine (*Fluka*; 1.16 ml, 5.82 mmol), followed by recrystallization from *i*-Pr₂O/hexane 1:2, yielded 1.97 g (93.7%) of (*S*)-**8a**. Pale brown powder. M.p. 115°. [α]_D = +33.7 (*c* = 0.7, CHCl₃); ee 99.8%. IR (KBr): 3417 *m* (br.), 1717 *s*, 1633 *s*, 1611 *m*, 1542 *m*, 1398 *m*, 1253 *w*, 1212 *w*, 735 *w*, 695 *w*. ¹H-NMR ((D₆)DMSO, 250 MHz): 7.44 (*m*, 1 fur. H); 7.31 (*m*, 5 arom. H); 6.75 (br. *s*, 1 NH); 6.29 (*m*, 1 fur. H); 6.03 (*m*, 1 fur. H); 4.98 (*s*, PhCH₂); 3.92 (*m*, 1 aliph. H); 3.10 (*dd*, *J* = 14.9, 4.9, 1 aliph. H); 2.87 (*m*, 3 aliph. H); 1.93–1.55 (*m*, 11 aliph. H); 1.34–1.05 (*m*, 11 aliph. H). MS: 288.3 (100, [*M* – H]⁺). Anal. calc. for C₂₇H₃₈N₂O₅ (470.610): C 68.91, H 8.14, N 5.95; found: C 68.58, H 8.43, N 5.78.

From (*S*)-**3a** (1.0 g, 3.29 mmol) in THF/H₂O/MeOH (100 ml) according to *Method D*: 1.45 g (95.9%) of (*S*)-**8a**; ee 99.2%.

Dicyclohexylammonium (*R*)-2-[(*Benzyloxy*)carbonylamino]-3-(*fur*-2-yl)propanoate ((*R*)-**8a**). From (*R*)-**4a** (1.34 g, 3.8 mmol) in CH₂Cl₂/H₂O/CF₃COOH (50 ml) according to *Method E*: 1.34 g (100%) of oily (*R*)-**7a** [26]; ee 98.9%. Further conversion using dicyclohexylamine (1.0 ml, 5.03 mmol), followed by recrystallization from *i*-Pr₂O/hexane 1:2, yielded 1.41 g (79%) of (*R*)-**8a**. Pale brown powder. M.p. 115°. [α]_D = –34.5 (*c* = 1.0, CHCl₃); ee 99.3%. IR, ¹H-NMR, MS: identical to those of (*S*)-**8a**. Anal. calc. for C₂₇H₃₈N₂O₅ (470.610): C 68.91, H 8.14, N 5.95; found: C 68.56, H 8.35, N 5.75.

From (*R*)-**3a** (1.3 g, 4.3 mmol) in THF/H₂O/MeOH (100 ml) according to *Method D*: 1.3 g (64.5%) of (*R*)-**8a**; ee 99.1%.

Dicyclohexylammonium (*S*)-2-[(*Benzyloxy*)carbonylamino]-3-(*fur*-3-yl)propanoate ((*S*)-**8b**). From (*S*)-**3b** (1.45 g, 4.78 mmol) in THF/H₂O/MeOH (180 ml), according to *Method D*: 0.585 g (26%) of (*S*)-**8b**. White powder. M.p. 150°. [α]_D = +35.1 (*c* = 1.00, CHCl₃); ee 99.5%. ¹H-NMR ((D₆)DMSO, 250 MHz): 7.47 (*m*, 1 fur. H); 7.32 (*m*, 5 arom. H, 1 fur. H); 6.66 (br. *s*, 1 NH); 6.29 (*m*, 1 fur. H); 4.98 (*s*, PhCH₂); 3.81 (*m*, 1 aliph. H); 2.86 (*m*, 2 aliph. H); 2.74 (*m*, 2 aliph. H); 1.93–1.55 (*m*, 10 aliph. H); 1.34–1.05 (*m*, 10 aliph. H). MS: 288.2 (100, [*M* – H]⁺). Anal. calc. for C₂₇H₃₈N₂O₅ (470.610): C 68.91, H 8.14, N 5.95; found: C 68.69, H 8.18, N 5.94.

Dicyclohexylammonium (*S*)-2-[(*Benzyloxy*)carbonylamino]-3-(*thiophen*-3-yl)propanoate ((*S*)-**8d**). From (*S*)-**3d** (0.80 g, 2.5 mmol) in THF/H₂O/MeOH (25 ml), according to *Method D*: 0.943 g (77.9%) of (*S*)-**8d**. White powder. M.p. 157.3°. [α]_D = +43.0 (*c* = 1.00, CHCl₃); ee 98.9%. ¹H-NMR ((D₆)DMSO, 250 MHz): 7.32 (*m*, 5 arom. H, 1 thioph. H); 7.05 (*m*, 1 thioph. H); 6.92 (*m*, 1 thioph. H); 6.67 (*d*, *J* = 7.9, 1 NH); 4.98 (*s*, 2 aliph. H); 3.87 (*m*, 1 aliph. H); 3.09 (*dd*, *J* = 14.9, 5.8, 1 aliph. H); 2.89 (*m*, 3 aliph. H); 1.92–1.56 (*m*, 10 aliph. H); 1.34–1.05 (*m*, 10 aliph. H). MS: 304.1 (100, [*M* – H]⁺). Anal. calc. for C₂₇H₃₈N₂O₄S (486.671): C 66.64, H 7.87, N 5.76, S 6.59; found: C 66.58, H 7.77, N 5.58, S 6.59.

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