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-αβ-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-αβ-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-αβ-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 CF_3CO_2H without any racemization.

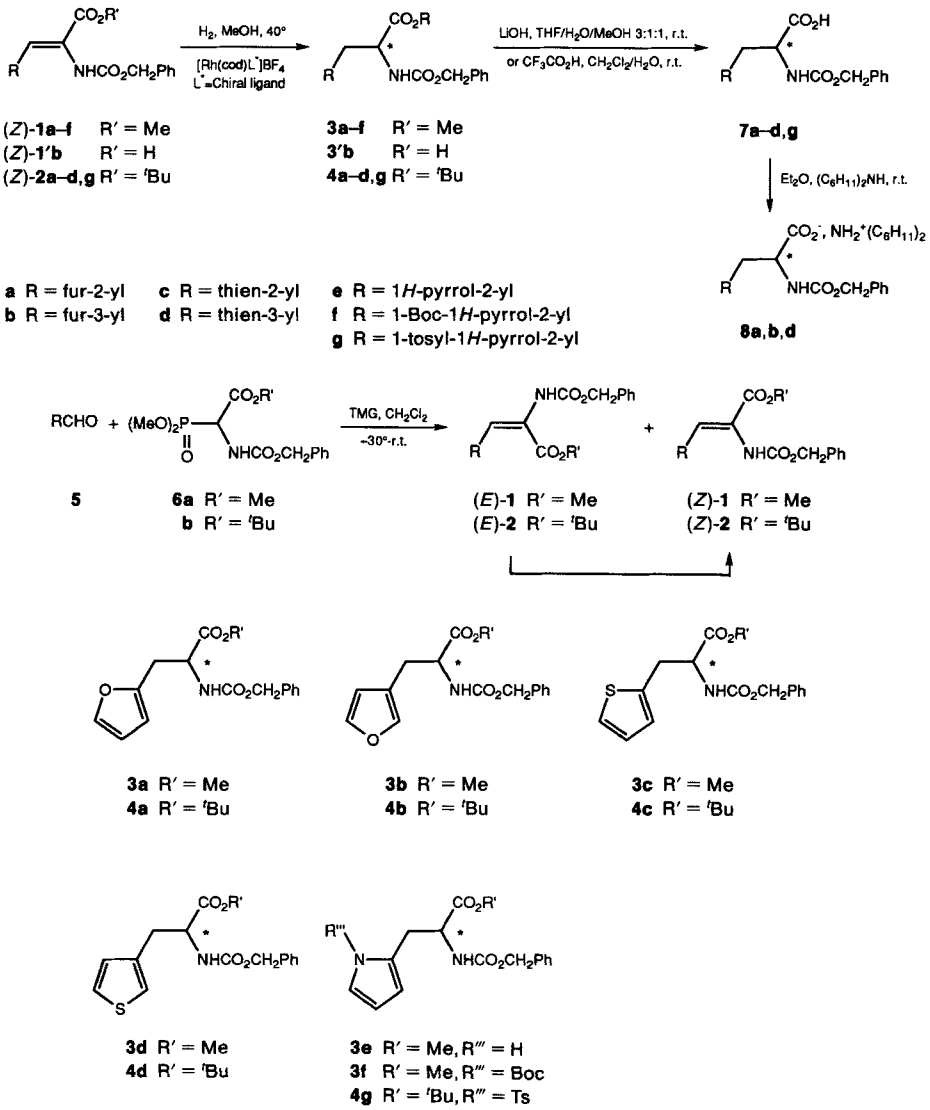
1. Introduction. – There is currently much interest in the synthesis, conformational properties, and pharmacology of α-amino acids, in particular non-coded amino acids. Consequently, several efforts focus on the development of new enantioselective methodologies for the synthesis of novel D- and L-α-amino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

In this paper, we describe a short and efficient method for the preparation of a range of enantiomerically highly pure five-membered heteroaryl analogues of phenylalanine of type **3** and **4**. Their synthesis is based on the asymmetric hydrogenation of the corresponding methyl and *tert*-butyl (*Z*)-α- amino-α,β- didehydro esters **1** and **2**, using diphosphinerhodium catalysts (*Scheme 1*). The esters **1** and **2** were synthesized using a modified

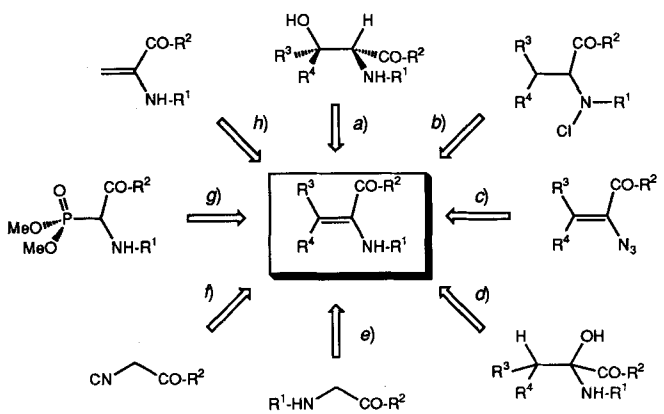
Scheme 1



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-α,β-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(4*H*)-ones [16]; *f*) by condensation of isocyanoacetates or isothiocyanoacetates 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].

Scheme 2



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-α,β-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-α,β-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 CH_2Cl_2 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 CH_2Cl_2 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-αβ-didehydro Esters* **1** *and* **2**, *Respectively*

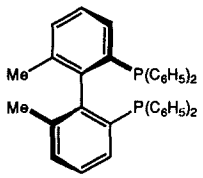
	Aldehyde	Solvent	Temp. [°C]	Product	(*E*/*Z*) Ratio	[%] of (*Z*)
Me Ester **6a**	**5a**	CH_2Cl_2	−30 to r.t.	**1a**	2:98	95.8
	5b	CH_2Cl_2	−30 to r.t.	**1b**	2:98	91.5
	5c	CH_2Cl_2	−30 to r.t.	**1c**	2:98	84.0
	5d	CH_2Cl_2	−30 to r.t.	**1d**	2:98	95.2
	5e	CH_2Cl_2	−30 to r.t.	**1e**	17:83	48
	5e	THF	−70 to r.t.	**1e**	17:83	56
	5f	CH_2Cl_2	−30 to r.t.	**1f**	17:83	60
Bu Ester **6b**	**5a**	CH_2Cl_2	−30 to r.t.	**2a**	5/95 ((*Z*) > 99)[a])	86.5
	5b	CH_2Cl_2	−30 to r.t.	**2b**	5/95 ((*Z*) > 99)[a])	87.4
	5c	CH_2Cl_2	−30 to r.t.	**2c**	5:95 (4:96)[a])	64.8
	5d	CH_2Cl_2	−30 to r.t.	**2d**	5:95 (4:96)[a])	81.2
	5f	CH_2Cl_2	−30 to r.t.	**2f**	42:58	
	5f	CH_2Cl_2	r.t.	**2f**	20:80	22
	5f	Dioxane	r.t.	**2f**	15:85	32
	5g	DME	−30 to r.t.	**2g**	13:87 ((*Z*) > 99)[a])	64.9

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

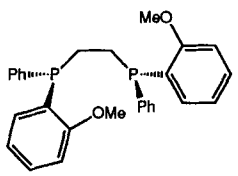
The required racemic phosphorylglycine *tert*-butyl ester **6b** was efficiently synthesized from **6a** in 70% overall yield by selective hydrolysis (2N aqueous NaOH, dioxane) followed by re-esterification (see *Exper. Part*). Subsequent coupling with aldehydes **5a–d**, **f**, **g** in CH_2Cl_2 with 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 $CHCl_3$/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 Et_2O/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*).

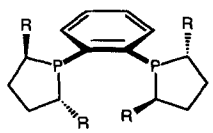
3. Asymmetric Hydrogenation of the (*Z*)-2-(Acylamino)-3-(heteroaryl)acrylates (*Z*)-1 and (*Z*)-2. – The key reaction for our synthesis of optically pure D- and L-(heteroaryl)alanine is the asymmetric hydrogenation of the esters (*Z*)-**1a–f** and (*Z*)-**2a–d, g** using chiral cationic diphosphinerhodium 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**.



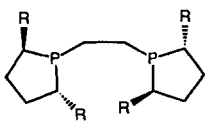
Ia (*R*)-config. (shown)
b (*S*)-config.



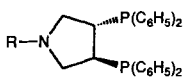
IIa (*R,R*)-config. (shown)
b (*S,S*)-config.



IIIa (all-*R*)-config., R = Me (shown)
b (all-*S*)-config., R = Me
c R = Et
d R = Pr
e R = i-Pr



IV R = Me, Et, Pr, i-Pr



V (*S,S*)-config., R = $PhCH_2$ (shown)

The asymmetric hydrogentions of the esters (*Z*)-**1a–f** and **2a–d, g** were performed in MeOH using Rh complexes [Rh(cod)ligand]BF_4 (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 $[Rh(cod)_2]BF_4$ in an equimolar ratio. All hydrogenations were carried out to complete conversion at 40° under 60 bar of H_2 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** (*R,R*)	1000	**3a**		85.5	(*S*)
	IIIb (all-*S*)	100		82.6	98.8	(*S*)
	IIIa (all-*R*)	100		99	98.4	(*R*)
(*Z*)-**1b**	**Ia** (*R*)	100	**3b**		12	(*R*)
	IIa (*R,R*)	1000			91	(*S*)
	IIIb (all-*S*)	100		97	97.5	(*S*)
	IIIa (all-*R*)	100		96	97.9	(*R*)
(*Z*)-**1c**	**IIa** (*R,R*)	1000	**3c**		90.5	(*S*)
	IIIb (all-*S*)	100		99	98.1	(*S*)
	IIIa (all-*R*)	100		93.5	98.0	(*R*)
(*Z*)-**1d**	**IIa** (*R,R*)	1000	**3d**		90.0	(*S*)
	IIIb (all-*S*)	100		99	96.5	(*S*)
	IIIa (all-*R*)	100		98	96.5	(*R*)
	IIIb (all-*S*)	500			96.5	(*S*)
	IIIb (all-*S*)	1000			96.2	(*S*)
(*Z*)-**1e**	**IIIb** (all-*S*)	100	**3e**	62.2	94.5	(*S*)
	IIIa (all-*R*)	100			94.5	(*R*)
(*Z*)-**1f**	**IIIb** (all-*S*)	100	**3f**	97.4	97.2	(*S*)
(*Z*)-**1'b**[b])	**IIa** (*R,R*)	100	**3'b**[b])	45.8	100[c])	(*S*)
	IIIb (all-*S*)	100		62.0	98.8[c])	(*S*)

[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**

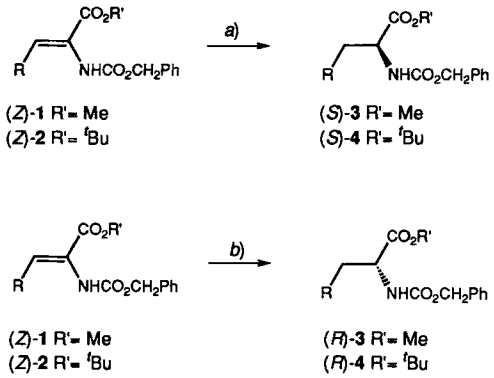
	Ligand	[2]/[C][a])	Product	Yield [%]	ee [%]	Abs. config.
(*Z*)-**2a**	**IIIb** (all-*S*)	100	**4a**	97.5	99.5	(*S*)
	IIIa (all-*R*)	100		80.0	99.6	(*R*)
(*Z*-**2b**	**IIIb** (all-*S*)	100	**4b**	90.0	98.9	(*S*)
	IIIa (all-*R*)	100		91.5	98.4	(*R*)
(*Z*)-**2c**	**IIIb** (all-*S*)	100	**4c**	96.5	99.0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

[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'b**; 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) H_2, MeOH, 40°, 60 bar, [Rh(cod)L*]BF_4; L* = **Ib** (*S*), **IIa** (*R,R*), **IIIb** (all-*S*). *b*) H_2, MeOH, 40°, 60 bar, [Rh(cod)L*]BF_4; 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/H_2O 3:1:1 and of **4** by treatment with aqueous CF_3CO_2H 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 [%]
(*S*)-**4b**	CF_3CO_2H	(*S*)-**7b**	79.5	99.1
(*R*)-**4b**	CF_3CO_2H	(*R*)-**7b**	82.5	98.6
(*S*)-**4c**	CF_3CO_2H	(*S*)-**7c**	87.2	99.4
(*R*)-**4c**	CF_3CO_2H	(*R*)-**7c**	83.7	98.9
(*S*)-**4d**	CF_3CO_2H	(*S*)-**7d**	90.5	99.8
(*R*)-**4d**	CF_3CO_2H	(*R*)-**7d**	89.0	99.5
(*S*)-**4g**	CF_3CO_2H	(*S*)-**7g**	76.8	99.0
(*R*)-**4g**	CF_3CO_2H	(*R*)-**7g**	82.6	99.0
(*S*)-**4a**	CF_3CO_2H	(*S*)-**7a**	93.7	99.5 (99.8)[b])
(*S*)-**3a**	LiOH	(*S*)-**7a**	95.9	97.4 (99.2)[b])
(*R*)-**4a**	CF_3CO_2H	(*R*)-**7a**	79.0[a])	98.9 (99.3)[b])
(*R*)-**3a**	LiOH	(*R*)-**7a**	64.5[a])	97.6 (99.1)[b])
(*S*)-**3b**	LiOH	(*S*)-**7b**	26.0[a])	95.6 (99.5)[b])
(*S*)-**3d**	LiOH	(*S*)-**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*-benzyloxycarbonyl-protected (*Z*)-α-amino-αβ-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 CF_3CO_2H 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. $[\alpha]_D$: *Perkin-Elmer 241* polarimeter; in $CDCl_3$, at r.t. ± 2°, unless otherwise specified. IR Spectra: *Nicolet-7199-FT* spectrophotometer; solids in KBr pellets, liquids as thin films; characteristic bands in cm^{-1}. ^1H-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 $CHCl_3$/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*)→(*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 [Rh(cod)ligand]BF_4 were prepared *in situ* by mixing the ligand **I**, **II**, or **IIIa**, **b** in MeOH with [Rh(cod)$_2$]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°/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 CH_2Cl_2/H_2O 9:0.3 (18.6 ml) was treated with CF_3CO_2H (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):

3295*m*, 3063*w*, 1731*s*, 1688*s*, 1623*s*, 1564*w*, 1511*s*, 1299*s*, 752*m*, 700*m*. ^{1}H-NMR ((D$_6$)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*, PhC*H*$_2$); 3.69 (*s*, MeO). MS: 301 (7, M^+), 193 (10), 107 (14), 106 (20), 91 (100), 79 (18). Anal. calc. for $C_{16}H_{15}NO_5$ (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 CH_2Cl_2 according to *Method A*: 5.74 g (91.5%) of (*Z*)-**1b**. M.p. 84.5°. IR (KBr): 3297*m*, 3063*w*, 1730*s*, 1699*s*, 1634*s*, 1555*w*, 1510*s*, 1271*s*, 752*m*, 700*m*. ^{1}H-NMR ((D$_6$)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*, PhC*H*$_2$); 3.70 (*s*, MeO). ^{13}C-NMR ((D$_6$)DMSO, 400 MHz): 52.61 (*q*, MeO): 65.94 (*t*, PhC*H*$_2$); 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*, *C*OOCH$_2$Ph); 165.33 (*s*, *C*OOMe). MS: 301 (6, M^+), 91 (100). Anal. calc. for $C_{16}H_{15}NO_5$ (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): 3303*m*, 3063*w*, 1709*s*, 1641*w*, 1561*m*, 1525*m*, 1260*s*, 1229*s*, 771*w*, 705*w*. ^{1}H-NMR ((D$_6$)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*, PhC*H*$_2$); 3.69 (*s*, MeO). MS: 301 (6, M^+), 106 (10), 91 (100). Anal. calc. for $C_{16}H_{15}NO_5$ (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 CH_2Cl_2 according to *Method A*: 3.58 g (84%) of (*Z*)-**1c**. M.p. 113.5°. IR (KBr): 3296*m*, 3063*w*, 1732*s*, 1693*s*, 1629*s*, 1498*s*, 1229*s*, 767*m*, 713*m*. ^{1}H-NMR ((D$_6$)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*, PhC*H*$_2$); 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 $C_{16}H_{15}NO_4S$ (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 CH_2Cl_2 according to *Method A*: 6.34 g (95.2%) of (*Z*)-**1d**. M.p. 90°. IR (KBr): 3288*m*, 3091*w*, 1730*s*, 1690*s*, 1626*s*, 1522*m*, 1284*s*, 1223*s*, 786*m*, 697*m*. ^{1}H-NMR ((D$_6$)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). ^{13}C-NMR ((D$_6$)DMSO, 400 MHz): 52.06 (*q*, MeO); 65.77 (*t*, PhC*H*$_2$O); 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*, *C*OOCH$_2$Ph); 165.52 (*s*, *C*OOMe). MS: 317 (10, M^+), 182 (10), 107 (14), 150 (12), 122 (18), 92 (10), 91 (100), 65 (10). Anal. calc. for $C_{16}H_{15}NO_4S$ (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 1*H*-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): 3419*m*, 3031*w*, 1707*s*, 1690*s*, 1640*s*, 1515*m*, 1506*w*, 1248*m*, 713*m*, 692*w*. ^{1}H-NMR ((D$_6$)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*, PhC*H*$_2$); 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 $C_{16}H_{16}N_2O_4$ (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]-1*H*-pyrrole-2-carbaldehyde (**5f**; 2.0 g, 10.3 mmol) in CH_2Cl_2 according to *Method A*: 2.46 g (60%) of (*Z*)-**1f**. M.p. 87.7°. IR (KBr): 3299*m*, 3143*w*, 1750*s*, 1727*s*, 1693*s*, 1630*s*, 1546*w*, 1522*m*, 1217*m*, 751*m*. ^{1}H-NMR ((D$_6$)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*, PhC*H*$_2$); 3.69 (*s*, MeO); 1.57 (*s*, *t*Bu). MS: 418.6 (65, $[M + NH_4]^+$), 401.4 (100, $[M + H]^+$). Anal. calc. for $C_{21}H_{24}N_2O_6$ (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/H$_2$O 5:1 (180 ml) was added LiOH·H$_2$O (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 H$_2$O and brine, dried (Na$_2$SO$_4$), and evaporated. The residue was chromatographed (SiO$_2$, CHCl$_3$/MeOH/H$_2$O 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): 3287*m* (br.), 2592*w* (br.), 1686*s*, 1647*s*, 1555*w*, 1511*m*, 1248*m*, 741*w*, 687*w*. ^{1}H-NMR ((D$_6$)DMSO, 250 MHz): 12.67 (br. *s*, CO$_2$H); 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*, PhC*H*$_2$). 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): 3284*m*, 1702*s*, 1641*m*, 1585*w*, 1519*s*, 1252*s*, 752*m*, 699*w*. ^{1}H-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): 3357*m*, 1734*s*, 1692*s*, 1652*s*, 1508*s*, 1238*s*, 775*m*, 736*m*. ^{1}H-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): 3275*m*, 1702*s*, 1633*s*, 1585*w*, 1517*s*, 1255*s*, 737*m*, 698*m*. ^{1}H-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): 3292*m*, 1701*s*, 1644*m*, 1585*w*, 1523*s*, 1251*s*, 738*m*, 697*m*. ^{1}H-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 (10). 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**. ^{1}H-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-1*H*-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): 3238*m*, 1717*s*, 1634*m*, 1595*w*, 1496*w*, 1336*m*, 1251*m*, 1156*s*, 732*m*, 701*m*. ^{1}H-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. $[\alpha]_D$ = + 49.1 (*c* = 1.00, $CHCl_3$); ee 98.8%. IR (film): 3341*m* (br.), 1724*s*, 1589*w*, 1509*s*, 1260*m*, 1214*m*, 738*m*, 698*m*. ^{1}H-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. $[\alpha]_D$ = – 50.2 (*c* = 1.00, $CHCl_3$); ee 98.4%. IR, ^{1}H-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. $[\alpha]_D$ = + 35.1 (*c* = 0.4, $CHCl_3$); ee 97.5%. IR (film): 3341*m* (br.), 1742*s*, 1582*w*, 1519*s*, 1213*m*, 1179*m*, 738*w*, 698*w*. ^{1}H-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**)]BF_4, according to *Method C:* 0.193 g (96%) of (*R*)-**3b**. Oil. $[\alpha]_D = -32.1$ ($c = 0.5$, $CHCl_3$); ee 97.9%. IR, ^{1}H-NMR, MS: identical to those of (*S*)-**3b**. Anal. calc. for $C_{16}H_{17}NO_5$ (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**)]BF_4, according to *Method C:* 0.20 g (99%) of (*S*)-**3c**. Oil. $[\alpha]_D = +55.6$ ($c = 0.5$, $CHCl_3$); ee 98.1%. IR (film): 3338*m* (br.), 1735*s*, 1722*s*, 1587*w*, 1516*s*, 1275*s*, 1212*s*, 739*w*, 698*m*. ^{1}H-NMR ((D_6)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*, PhCH_2); 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 $C_{16}H_{17}NO_4S$ (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**)]BF_4, according to *Method C:* 0.188 g (93.5%) of (*R*)-**3c**. Oil. $[\alpha]_D = -55.4$ ($c = 0.5$, $CHCl_3$); ee 98.0%. IR, ^{1}H-NMR, MS: identical to those of (*S*)-**3c**. Anal. calc. for $C_{16}H_{17}NO_4S$ (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**)]BF_4, according to *Method C:* 0.199 g (99%) of (*S*)-**3d**. Oil. $[\alpha]_D = +46.1$ ($c = 0.5$, $CHCl_3$); ee 96.5%. IR (film): 3342*m* (br.), 1735*s*, 1723*s*, 1583*w*, 1520*s*, 1261*s*, 1213*s*, 773*w*, 698*m*. ^{1}H-NMR ((D_6)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*, PhCH_2); 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 $C_{16}H_{17}NO_4S$ (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**)]BF_4, according to *Method C:* 0.197 g (98%) of (*R*)-**3d**. Oil. $[\alpha]_D = -45.0$ ($c = 0.5$, $CHCl_3$); ee 96.5%. IR, ^{1}H-NMR, MS: identical to those of (*S*)-**3d**. Anal. calc. for $C_{16}H_{17}NO_4S$ (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**)]BF_4, according to *Method C:* 0.125 g (62.2%) of (*S*)-**3e**. Oil. $[\alpha]_D = +27.4$ ($c = 0.5$, $CHCl_3$); ee 94.5%. IR (film): 3370*m* (br.), 1714*s*, 1582*w*, 1515*s*, 1256*s*, 1216*s*, 726*w*, 699*m*. ^{1}H-NMR ((D_6)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 $C_{16}H_{18}N_2O_4$ (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**)]BF_4, 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): 3367*m* (br.), 1739*s*, 1715*s*, 1582*w*, 1521*s*, 1248*s*, 1213*s*, 730*w*, 697*m*. ^{1}H-NMR ((D_6)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*, PhCH_2); 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 $C_{21}H_{26}N_2O_6$ (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**)]BF_4, according to *Method C:* 1.57 g (97.5%) of (*S*)-**4a**. Oil. $[\alpha]_D = +41.2$ ($c = 1.00$, $CHCl_3$); ee 99.5%. IR (film): 3340*m* (br.), 1721*s*, 1598*w*, 1505*s*, 1221*s*, 1156*s*, 736*m*, 698*m*. ^{1}H-NMR ((D_6)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*, PhCH_2); 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), 81 (20), 65 (14), 57 (40), 53 (10), 41 (16), 39 (12). Anal. calc. for $C_{19}H_{23}NO_5$ (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**)]BF_4, according to *Method C:* 1.61 g (80%) of (*R*)-**4a**. Oil. $[\alpha]_D = -41.2$ ($c = 1.00$, $CHCl_3$); ee 99.6%. IR, ^{1}H-NMR, MS: identical to those of (*S*)-**4a**. Anal. calc. for $C_{19}H_{23}NO_5$ (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**)]BF_4, according to *Method C:* 1.81 g (90%) of (*S*)-**4b**. Oil. $[\alpha]_D = +29.2$ ($c = 1.00$, $CHCl_3$); ee 98.9%. IR (film): 3402*m* (br.), 1741*s*, 1700*s*, 1588*w*, 1521*s*, 1251*s*, 1150*s*,

754*m*, 698*m*. ^{1}H-NMR ((D$_6$)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*, PhC*H*$_2$); 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 $C_{19}H_{23}NO_5$ (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**)]BF$_4$, according to *Method C*: 1.84 g (91.5%) of (*R*)-**4b**. Oil. $[\alpha]_D$ = −30.9 (*c* = 1.00, CHCl$_3$); ee 98.4%. IR, ^{1}H-NMR, MS: identical to those of (*S*)-**4b**. Anal. calc. for $C_{19}H_{23}NO_5$ (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**)]BF$_4$, according to *Method C*: 1.94 g (96.5%) of (*S*)-**4c**. Oil. $[\alpha]_D$ = +43.6 (*c* = 1.00, CHCl$_3$); ee 99.0%. IR (film): 3346*m* (br.), 1724*s*, 1585*w*, 1504*m*, 1244*s*, 1220*s*, 750*w*, 697*m*. ^{1}H-NMR ((D$_6$)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*, PhC*H*$_2$); 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 $C_{19}H_{23}NO_4S$ (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**)]BF$_4$, according to *Method C*: 2.88 g (98.5%) of (*R*)-**4c**. Oil. $[\alpha]_D$ = −43.5 (*c* = 1.00, CHCl$_3$); ee 99.1%. IR, ^{1}H-NMR, MS: identical to those of (*S*)-**4c**. Anal. calc. for $C_{19}H_{23}NO_4S$ (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**)]BF$_4$, according to *Method C*: 0.631 g (99.5%) of (*S*)-**4d**. M.p. 83.5°. $[\alpha]_D$ = +40.2 (*c* = 0.9, CHCl$_3$); ee 98.4%. IR (KBr): 3395*m* (br.), 1740*s*, 1698*s*, 1583*w*, 1517*s*, 1267*m*, 1217*m*, 752*w*, 698*m*. ^{1}H-NMR ((D$_6$)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 (10), 97 (18), 91 (100), 65 (12), 57 (36), 41 (14), 39 (10). Anal. calc. for $C_{19}H_{23}NO_4S$ (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**)]BF$_4$, according to *Method C*: 2.2 g (99.5%) of (*R*)-**4d**. M.p. 83°. $[\alpha]_D$ = −39.5 (*c* = 1.00, CHCl$_3$); ee 98.4%. IR, ^{1}H-NMR, MS: identical to those of (*S*)-**4d**. Anal. calc. for $C_{19}H_{23}NO_4S$ (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]-1*H*-pyrrol-2-yl}propanoate* ((*S*)-**4g**). From (*Z*)-**2g** (2.0 g, 4.03 mmol) in MeOH (20 ml), using [Rh(cod)(**IIIb**)]BF$_4$, according to *Method C*: 1.8 g (90.5%) of (*S*)-**4g**. Oil. $[\alpha]_D$ = +12.2 (*c* = 0.6, CHCl$_3$); ee 99.1%. IR (film): 3392*m* (br.), 1724*s*, 1596*w*, 1518*m*, 1367*s*, 1227*s*, 1175*s*, 720*m*, 672*m*. ^{1}H-NMR ((D$_6$)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*, PhC*H*$_2$); 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 $C_{26}H_{30}N_2O_6S$ (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]-1*H*-pyrrol-2-yl}propanoate* ((*R*)-**4g**). From (*Z*)-**2g** (1.03 g, 2.67 mmol) in MeOH (15 ml), using [Rh(cod)(**IIIa**)]BF$_4$, according to *Method C*: 0.98 g (95.2%) of (*R*)-**4g**. Oil. $[\alpha]_D$ = −10.8 (*c* = 0.5, CHCl$_3$); ee 98.5%. IR, ^{1}H-NMR, MS: identical to those of (*S*)-**4g**. Anal. calc. for $C_{26}H_{30}N_2O_6S$ (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]-1*H*-pyrrole-2-carbaldehyde* (**5f**). To a stirred soln. of **5e** (1.0 g, 1.05 mmol) in CH_2Cl_2 (100 ml) were added under Ar, at r.t., a catalytic amount of DMAP, (i-Pr)$_2$EtN (*Fluka*; 2.34 ml, 13.7 mmol), and di(*tert*-butyl) dicarbonat (*Fluka*; 2.98 g, 13.7 mmol). The mixture was quenched with 1N aq. $KHSO_4$, extracted with $CHCl_3$, the combined org. layer washed with brine (10 ml), dried (Na_2SO_4), and evaporated, and the residue chromatographed (SiO_2, AcOEt/hexane/$CHCl_3$ 1:3:1): **5f** (1.88 g, 91.7%). Yellow oil. IR (film): 3175*w*, 1749*s*, 1668*s*, 1544*m*, 1166*s*, 1126*s*. ^{1}H-NMR ($CDCl_3$, 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 $C_{10}H_{13}NO_3$ (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]-1*H*-pyrrole-2-carbaldehyde* (**5g**). As described for **5f**, with **5e** (5.0 g, 52 mmol), $CHCl_2$ (200 ml), cat. DMAP, (i-Pr)$_2$EtN (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): 3124*w*, 1666*s*, 1594*m*, 1530*m*, 1489*m*, 1365*s*, 1175*s*, 1153*s*, 810*w*, 777*m*, 752*m*. ^{1}H-NMR ((D$_6$)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 $C_{12}H_{11}NO_3S$ (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-[(Benzyloxy)carbonylamino]-3-(furan-3-yl)propanoic Acid ((*S*)-**7b**). From (*S*)-**4b** (1.10 g, 3.18 mmol) in $CH_2Cl_2/H_2O/CF_3COOH$ (36 ml) according to *Method E:* 0.731 g (79.5%) of (*S*)-**7b**. White powder. M.p. 78°. $[\alpha]_D = +39.5$ (*c* = 1.00, $CHCl_3$); ee 99.1%. IR (KBr): 3339*m* (br.), 1722*s*, 1701*s*, 1665*s*, 1585*w*, 1527*s*, 1265*s*, 1236*s*, 736*w*, 698*w*. ^{1}H-NMR ((D$_6$)DMSO, 250 MHz): 12.73 (br. *s*, CO_2H); 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*, PhCH_2); 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 $C_{15}H_{15}NO_5$ (289.287): C 62.28, H 5.23, N 4.84; found: C 62.10, H 5.38, N 4.77.

(R)-2-[(Benzyloxy)carbonylamino]-3-(furan-3-yl)propanoic Acid ((*R*)-**7b**). From (*R*)-**4b** (1.10 g, 3.18 mmol) in $CH_2Cl_2/H_2O/CF_3COOH$ (36 ml) according to *Method E:* 0.759 g (82.5%) of (*R*)-**7b**. White powder. M.p. 78°. $[\alpha]_D = -37.5$ (*c* = 1.00, $CHCl_3$); ee 98.6%. IR, ^{1}H-NMR, MS: identical to those of (*S*)-**7b**. Anal. calc. for $C_{15}H_{15}NO_5$ (289.287): C 62.28, H 5.23, N 4.84; found: C 62.35, H 5.55, N 4.79.

(S)-2-[(Benzyloxy)carbonylamino]-3-(thiophen-2-yl)propanoic Acid [26] ((*S*)-**7c**). From (*S*)-**4c** (0.617 g, 1.70 mmol) in $CH_2Cl_2/H_2O/CF_3COOH$ (21.7 ml) according to *Method E:* 0.454 g (87.2%) of (*S*)-**7c**. White powder. M.p. 86.5°. $[\alpha]_D = +49.0$ (*c* = 1.00, $CHCl_3$); ee 99.4%. IR (KBr): 3330*m* (br.), 1715*s*, 1699*s*, 1669*s*, 1583*w*, 1531*s*, 1225*m*, 735*w*, 684*w*. ^{1}H-NMR ((D$_6$)DMSO, 250 MHz): 12.86 (br. *s*, CO_2H); 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*, PhCH_2); 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 $C_{15}H_{15}NO_4S$ (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-[(Benzyloxy)carbonylamino]-3-(thiophen-2-yl)propanoic Acid [26] ((*R*)-**7c**). From (*R*)-**4c** (1.40 g, 3.87 mmol) in $CH_2Cl_2/H_2O/CF_3COOH$ (50.5 ml) according to *Method E:* 0.988 g (83.7%) of (*R*)-**7c**. White powder. M.p. 86.5°. $[\alpha]_D = -49.3$ (*c* = 1.00, $CHCl_3$); ee 98.9%. IR, ^{1}H-NMR, MS: identical to those of (*S*)-**7c**. Anal. calc. for $C_{15}H_{15}NO_4S$ (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-[(Benzyloxy)carbonylamino]-3-(thiophen-3-yl)propanoic Acid [26] ((*S*)-**7d**). From (*S*)-**4d** (0.87 g, 2.4 mmol) in $CH_2Cl_2/H_2O/CF_3COOH$ (36 ml) according to *Method E:* 0.662 g (90.5%) of (*S*)-**7d**. White powder. M.p. 90°. $[\alpha]_D = +54.2$ (*c* = 1.00, $CHCl_3$); ee 99.8%. IR (KBr): 3324*m* (br.), 1715*s*, 1698*s*, 1668*s*, 1585*w*, 1531*s*, 1263*m*, 1223*m*, 784*w*, 696*w*. ^{1}H-NMR ((D$_6$)DMSO, 250 MHz): 12.75 (br. *s*, CO_2H); 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*, PhCH_2); 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, $[M + NH_4]^+$). Anal. calc. for $C_{15}H_{15}NO_4S$ (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-[(Benzyloxy)carbonylamino]-3-(thiophen-3-yl)propanoic Acid [26] ((*R*)-**7d**. From (*S*)-**4d** (1.07 g, 2.96 mmol) in $CH_2Cl_2/H_2O/CF_3COOH$ (36 ml) according to *Method E:* 0.804 g (89%) of (*R*)-**7d**. White powder. M.p. 89.5°. $[\alpha]_D = -51.3$ (*c* = 1.00, $CHCl_3$); ee 99.5%. IR, ^{1}H-NMR, MS: identical to those of (*S*)-**7d**. Anal. calc. for $C_{15}H_{15}NO_4S$ (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-[(Benzyloxy)carbonylamino]-3-{1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrol-2-yl}propanoic Acid* [26] ((*S*)-**7g**). From (*S*)-**4g** (0.90 g, 1.8 mmol) in $CH_2Cl_2/H_2O/CF_3COOH$ (36 ml) according to *Method E:* 0.613 g (76.8%) of (*S*)-**7g**. White powder. M.p. 84.5°. $[\alpha]_D = -6.2$ (*c* = 1.00, $CHCl_3$); ee 99.0%. IR (KBr): 3410*m* (br.), 1722*s*, 1590*w*, 1527*s*, 1366*s*, 1215*m*, 1175*m*, 805*w*, 678*w*. ^{1}H-NMR ((D$_6$)DMSO, 250 MHz): 12.77 (br. *s*, CO_2H); 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*, PhCH_2); 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, $[M + NH_4]^+$). Anal. calc. for $C_{22}H_{22}N_2O_6S$ (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-[(Benzyloxy)carbonylamino]-3-{1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrol-2-yl}propanoic Acid* ((*R*)-**7g**). From (*R*)-**4g** (0.87 g, 1.74 mmol) in $CH_2Cl_2/H_2O/CF_3COOH$ (35 ml) according to *Method E:* 0.635 g (82.6%) of (*R*)-**7g**. White powder. M.p. 84.5°. $[\alpha]_D = +6.7$ (*c* = 1.00, $CHCl_3$); ee 99.0%. IR, ^{1}H-NMR, MS: identical to those of (*S*)-**7g**. Anal. calc. for $C_{22}H_{22}N_2O_6S$ (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-[(Benzyloxy)carbonylamino]-3-(furan-2-yl)propanoate ((*S*)-**8a**). From (*S*)-**4a** (1.55 g, 4.48 mmol) in $CH_2Cl_2/H_2O/CF_3COOH$ (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-Pr_2O/hexane 1:2, yielded 1.97 g (93.7%) of (*S*)-**8a**. Pale brown powder. M.p. 115°. $[\alpha]_D = +33.7$ ($c = 0.7$, $CHCl_3$); 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*. ^{1}H-NMR ((D_6)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*, $PhCH_2$); 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 $C_{27}H_{38}N_2O_5$ (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/H_2O/MeOH (100 ml) according to *Method D:* 1.45 g (95.9%) of (*S*)-**8a**; ee 99.2%.

Dicyclohexylammonium (R)-2-[(Benzyloxy)carbonylamino]-3-(furan-2-yl)propanoate ((*R*)-**8a**). From (*R*)-**4a** (1.34 g, 3.8 mmol) in CH_2Cl_2/H_2O/CF_3COOH (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-Pr_2O/hexane 1:2, yielded 1.41 g (79%) of (*R*)-**8a**. Pale brown powder. M.p. 115°. $[\alpha]_D = -34.5$ ($c = 1.0$, $CHCl_3$); ee 99.3%. IR, ^{1}H-NMR, MS: identical to those of (*S*)-**8a**. Anal. calc. for $C_{27}H_{38}N_2O_5$ (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/H_2O/MeOH (100 ml) according to *Method D:* 1.3 g (64.5%) of (*R*)-**8a**; ee 99.1%.

Dicyclohexylammonium (S)-2-[(Benzyloxy)carbonylamino]-3-(furan-3-yl)propanoate ((*S*)-**8b**). From (*S*)-**3b** (1.45 g, 4.78 mmol) in THF/H_2O/MeOH (180 ml), according to *Method D:* 0.585 g (26%) of (*S*)-**8b**. White powder. M.p. 150°. $[\alpha]_D = +35.1$ ($c = 1.00$, $CHCl_3$); ee 99.5%. ^{1}H-NMR ((D_6)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*, $PhCH_2$); 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 $C_{27}H_{38}N_2O_5$ (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/H_2O/MeOH (25 ml), according to *Method D:* 0.943 g (77.9%) of (*S*)-**8d**. White powder. M.p. 157.3°. $[\alpha]_D = +43.0$ ($c = 1.00$, $CHCl_3$); ee 98.9%. ^{1}H-NMR ((D_6)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 $C_{27}H_{38}N_2O_4S$ (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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