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Asymmetric synthesis of α- and β-amino acids by diastereoselective addition of triorganozincates to *N*-(*tert*-butanesulfinyl)imines

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This paper is dedicated to Professor Henri B. Kagan on occasion of his 80th anniversary

ABSTRACT

The diastereoselective addition of triorganozincates to (*R*)-*N*-(*tert*-butanesulfinyl)imines has been used as a key step to achieve the synthesis of highly enantiomerically enriched N-protected α- and β-amino acids. Desulfinylation of the addition products followed by benzoylation of the nitrogen atom of the obtained primary amines and oxidation of one of the substituents on the carbon atom connected to the nitrogen complete the sequence. Using the same configuration in the sulfinyl chiral auxiliary, α-amino acids with the (*R*) or the (*S*) configuration can be prepared by choosing the proper combination of imine and organozincate. α,α-Disubstituted α-amino esters with high enantiomeric purity can also be prepared when α-imino esters are the starting substrates.

1. Introduction

Due to the importance of α-amino acids[1] as constituents of naturally occurring structures,[2] such as peptides and proteins, their asymmetric synthesis is still a very active research field in synthetic organic chemistry. α-Amino acids have found applications as building blocks for the preparation of agrochemical and pharmaceutical compounds[2] and are also used as chiral auxiliaries and catalysts in a variety of synthetic procedures.[3] The numerous methods available for the synthesis of optically active α-amino acids include several of them which rely on the stereoselective addition of carboxylate synthons to C=N bonds, such as the Strecker reaction or the Ugi condensation.[1a,b] Some alkenyl,[4] aryl[5] and heteroaryl[5d,6] substituents can be considered as synthetic equivalents for the carboxylic acid, since they can be oxidatively cleaved to that functional group. The addition of such oxidizable side chains to chiral imines mediated by organometallic reagents[4a,c,6b] or their introduction as substituents of the imine substrates[4b,5d,6a,d–f] is crucial in several synthetic methodologies for the preparation of α-amino acids found in the literature.

On the other hand, the synthesis of β-amino acids[7] has been the subject of study of many researchers since the discovery that their introduction into peptides enhances the stability of the latter against proteolytic enzymes,[8] which improves the metabolic lability of these peptides and allows their use as medicinal drugs. For instance, several of these β-peptides have shown antifungal[9] and antibacterial[10] activities. β-Amino acids are very useful as chiral building blocks and as precursors of β-lactams.[7b] Functionalized β-amino acids are components of several bioactive molecules, such as Taxol, one of the most active antitumour agents.[7a] The methodologies for the asymmetric preparation of β-amino acids include homologation of enantiopure α-amino acids, enantioselective Mannich reactions, enzymatic resolution, Curtius rearrangement, aminohydroxylation of α,β-unsaturated esters, stereoselective hydrogenation of β-aminoacrylic acid derivatives, enolate addition to chiral imines and conjugate addition of amines to α,β-unsaturated esters.[7]

We have recently reported the highly diastereoselective addition of triorganozincates to *N*-(*tert*-butanesulfinyl)imines,[11] which are very useful substrates for the preparation of chiral primary amines.[12] By using an excess of a previously formed triorganozincate, good yields and diastereoselectivities were obtained in the addition products, which could be easily transformed into the corresponding enantiomerically enriched amines by desulfinylation of the nitrogen atom. We have improved this method by using only a catalytic amount of a dialkylzinc to generate the organozincate,[11c] which has led to higher yields and diastereoselectivities than in the stoichiometric version. These results prompted us to apply our catalytic methodology to the preparation of chiral primary amines bearing oxidizable substituents, with the final aim of converting these amines into amino acids.[13] Herein, we report two different approaches that have allowed us to effect the asymmetric synthesis of α- and β-amino acids.[14]

2. Results and discussion

We have verified that the catalytic generation of a triorganozincate in the presence of a sulfinylimine generally gives a higher diastereoselectivity than the addition of an excess of the previously prepared triorganozincate to the imine.[11c,14] Therefore, we decided to use only the catalytic method to carry out this study. Since it is

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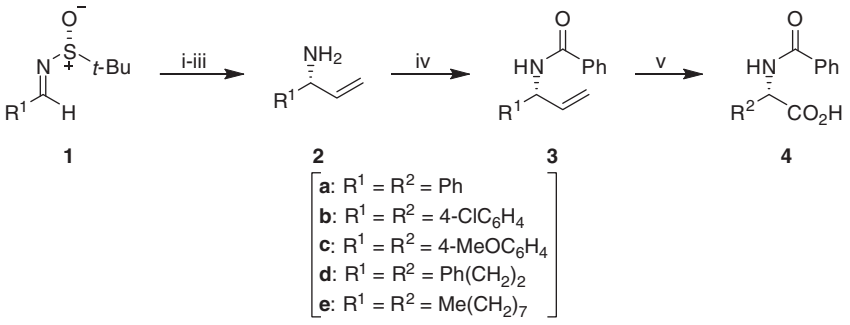
well known that the vinyl group can be oxidatively cleaved to the corresponding carboxylic acid,[4] we thought that the application of our methodology to the synthesis of α-branched allylamines **2** (Scheme 1) would offer us the opportunity to prepare enantiomerically enriched α-substituted α-amino acids after the oxidation step. Thus, the addition of the organozincate generated from CH_2=CHMgBr and a catalytic amount of Me_2Zn to benzaldimine **1a** gave the expected addition product, which was desulfinylated by reaction with a solution of HCl in methanol[15] and the obtained free primary amine **2a** was benzoylated with the aim of facilitating the isolation of the final amino acid. Treatment of the benzamide **3a** with $NaIO_4$ in the presence of a catalytic amount of $RuCl_3$ gave *N*-benzoyl (*S*)-phenylglycine **4a** with a 94% ee (Scheme 1, Table 1, entry 1). An optimization of the experimental conditions revealed that the best results were obtained performing the reaction in THF at −78 °C. The same sequence applied to the aromatic imines **1b** and **1c** gave the expected protected amino acids **4b** and **4c** with enantioselectivities of 92% and 88%, respectively (Scheme 1, Table 1, entries 2 and 3). Aliphatic imines **1d** and **1e** were also tested as substrates and afforded the expected amino acids **4d** and **4e** in good yields (Scheme 1, Table 1, entries 4 and 5), although the ees were lower than those obtained with the aromatic imines **1a**–**c**. It is worth noting that, since $Me_2(CH_2$=$CH)ZnMgBr$ and CH_2=CHMgBr have shown opposite diastereoselectivities in their addition to *N*-(*tert*-butanesulfinyl)benzaldimines,[11a,b,16] either enantiomer of the amino acid could be prepared by an appropriate selection of the nucleophile.

Since the oxidation of the furyl group to a carboxylic acid is also well documented in the literature,[4c,5c,6] we tried an alternative approach to amino acids with the (*R*) absolute configuration. The addition of primary and secondary alkyl groups to the heterocyclic imine **1f** (Scheme 2) through the corresponding alkyldimethylzincates gave the expected sulfinamides in high diastereomeric ratios, which were then converted into the corresponding primary amines **2**. After benzoylation of the nitrogen, the obtained benzamides **3** were submitted to oxidation with $NaIO_4$ catalyzed by $RuCl_3$, which transformed the furan ring into a carboxy group, leading to the expected *N*-benzoyl (*R*)-amino acids *ent*-**4fa**–**fe** in good yields and with ee values between 92% and 96% (Scheme 2, Table 1, entries 6–10). Since in this case the substituent that was oxidatively cleaved was not introduced in the nucleophilic addition step but it already was in the starting imine, the absolute configuration of the amino acid was opposite to the one obtained in our first approach (Scheme 1). Our methodology is complementary to other reported approaches to α-amino acids involving the stereoselective addition of organolithium[6a] or dialkylzinc[6e] reagents to imines derived from furfural, since we obtain the opposite enantiomer of the final amino acid.

We also tried to prepare α-amino acids with a quaternary stereogenic centre using α-imino ester 5 (Scheme 3) as starting

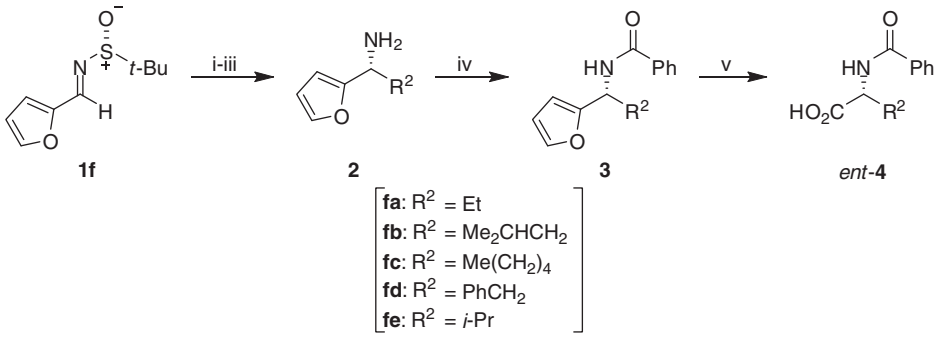


Scheme 1. Reagents and conditions: (i) CH_2=CHMgBr (1.3 equiv), Me_2Zn (0.15 equiv), THF, −78 °C; (ii) NH_4Cl (aq); (iii) HCl, MeOH; (iv) PhCOCl (2 equiv), 2 M NaOH (aq) (34 equiv), CH_2Cl_2, 0–20 °C. (v) $RuCl_3 \times H_2O$ (5 mol %), $NaIO_4$ (6 equiv), $MeCN/H_2O/CCl_4$ (3:3:2), 20 °C.

Table 1
Asymmetric synthesis of α-amino acids via the diastereoselective addition of triorganozincates to *N*-(*tert*-butanesulfinyl)imines

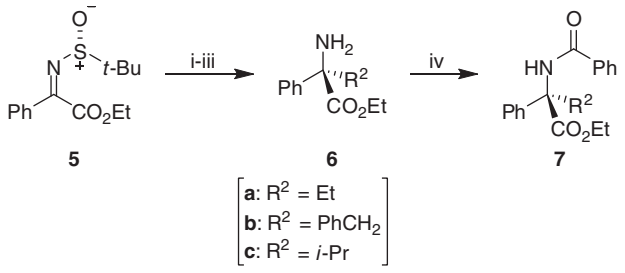
Entry	Imine	Amine		Benzamide			α-Amino acid			
		No.[a]	Yield[b] (%)	No.[a]	Yield[c] (%)	ee[d] (%)	No.[a]	R^2	Yield[e] (%)	ee[f] (%)
1	**1a**	**2a**	71	**3a**	87	96	**4a**	Ph	94	94
2	**1b**	**2b**	62	**3b**	92	92	**4b**	4-ClC_6H_4	89	92
3	**1c**	**2c**	65	**3c**	83	88	**4c**	4-$MeOC_6H_4$	96	88
4	**1d**	**2d**	34	**3d**	81	60	**4d**	$Ph(CH_2)_2$	90	58
5	**1e**	**2e**	47	**3e**	96	60	**4e**	$Me(CH_2)_7$	77	60
6	**1f**	**2fa**	62	**3fa**	60	94	*ent*-**4fa**	Et	75	92
7	**1f**	**2fb**	58	**3fb**	99	96	*ent*-**4fb**	Me_2CHCH_2	98	96
8	**1f**	**2fc**	59	**3fc**	99	92	*ent*-**4fc**	$Me(CH_2)_4$	77	92
9	**1f**	**2fd**	52	**3fd**	85	94	*ent*-**4fd**	$PhCH_2$	90	92
10	**1f**	**2fe**	65	**3fe**	69	95	*ent*-**4fe**	*i*-Pr	88	92
11	**5**	**6a**	54	**7a**	96	86	—	—	—	—
12	**5**[g]	**6a**	61	**7a**	96	92	—	—	—	—
13	**5**	**6b**	70	**7b**	74	80	—	—	—	—
14	**5**	**6c**	63	**7c**	84	62	—	—	—	—

[a] Product number corresponding to the major enantiomer.
[b] Overall isolated yield from the imine to the free amine based on the starting imine **1**.
[c] Isolated yield after column chromatography (hexane/ethyl acetate) based on the free amine **2**. All isolated compounds were ⩾95% pure (GC and/or 300 MHz ^1H NMR).
[d] Determined by HPLC using a ChiralCel OD-H column. The absolute configuration of the major enantiomer was deduced by comparison of the sign of the specific rotation of the free primary amine **2** with the reported data.
[e] Isolated yield based on the benzoylated amine **3**. All isolated compounds were ⩾95% pure (GC and/or 300 MHz ^1H NMR).
[f] Determined for the corresponding methyl ester by HPLC using a ChiralCel OD-H column.
[g] The reaction was performed at −100 °C.



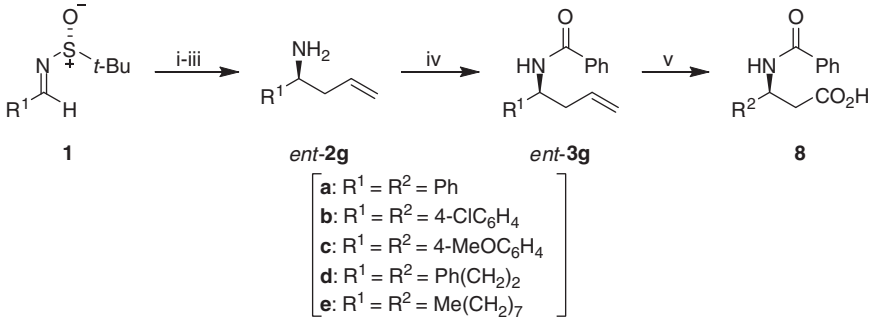
Scheme 2. Reagents and conditions: (i) R^2MgBr (1.3 equiv), Me_2Zn (0.15 equiv), THF, −78 °C; (ii) NH_4Cl (aq) (iii) HCl, MeOH; (iv) PhCOCl (2 equiv), 2 M NaOH (aq) (34 equiv), CH_2Cl_2, 0–20 °C. (v) $RuCl_3 \times H_2O$ (5 mol %), $NaIO_4$ (6 equiv), $MeCN/H_2O/CCl_4$ (3:3:2), 20 °C.

material. We first attempted the addition of $EtMe_2ZnMgBr$ to the imino ester at −78 °C. We were glad to see that the ethylation product was also obtained from the activated ketimine **5** and, after desulfinylation and benzoylation, afforded the protected amino ester **7a** with an 86% ee (Scheme 3, Table 1, entry 11). In an attempt to improve the stereoselectivity, the addition reaction was repeated at −100 °C, which led to the final amino ester with a 92% ee (Scheme 3, Table 1, entry 12). An interesting point to remark is that a reversal of the diastereoselectivity was observed when EtMgBr was added to **5** instead of the trialkylzincate [70% ee for the (*S*) enantiomer].[11b] Thus, both enantiomers of the final amino ester could be prepared from the same imine substrate just by changing the nucleophilic reagent. The addition of benzyl and isopropyl groups also proceeded very efficiently at −78 °C, giving the expected N-protected amino esters **7b** and **7c** in good yields, although with lower enantioselectivities than in the ethylation reaction (80% and 62% ee, respectively; Scheme 3, Table 1, entries 13 and 14). No improvement was observed in these two cases when the reaction was repeated at −100 °C. In all cases, the addition of the triorganozincate took place from the same face of the imino ester as for the additions to the aldimines, giving the (*R*) absolute configuration in the obtained α-amino esters **6** and **7**.



Scheme 3. Reagents and conditions: (i) EtMgBr (1.3 equiv), Me_2Zn (0.15 equiv), THF, −78 or −100 °C; (ii) NH_4Cl (aq); (iii) HCl, MeOH; (iv) PhCOCl (2 equiv), 2 M NaOH (aq) (34 equiv), CH_2Cl_2, 0–20 °C.

Next, we examined the possibility of applying our strategy to the synthesis of β-amino acids. Since the addition of the vinyl group to imines **1** successfully led to the expected α-amino acids, we thought that extending the chain of the nucleophile by one more carbon would allow us to prepare the homologous series. Thus, we tried to do the allylation of imine **1a** by treating it with the organozincate generated from $CH_2{=}CHCH_2MgBr$ and a catalytic amount of Me_2Zn in THF at −78 °C. The expected amine *ent*-**2ga** was obtained in good yield, but with a disappointing 44% ee. We performed several experiments at different temperatures with the aim of trying to improve the enantioselectivity and it increased by raising the reaction temperature, the results being as follows: 72% ee (at −40 °C), 80% ee (at 0 °C) and 90% ee (at 20 °C). No further improvement was obtained by setting up the reaction at 50 °C. Therefore, we chose 20 °C as the optimum temperature. The addition of the allyl group to **1a** at that temperature followed by desulfinylation yielded the expected homoallylamine *ent*-**2ga**, which was then protected at the nitrogen atom with the benzoyl group affording benzamide *ent*-**3ga** with 90% ee (Scheme 4, Table 2, entry 1). The oxidative cleavage of the terminal C=C bond was carried out by reaction with $NaIO_4$ catalyzed by $RuCl_3$, giving the desired β-amino acid **8a** in 91% yield and with an 88% ee. Imine **1b** could also be transformed into the protected amino acid **8b** with a 92% ee (Scheme 4, Table 2, entry 2). However, when we submitted the imine **8c**, derived from 4-methoxybenzaldehyde, to the same reaction sequence, amino aldehyde **9** (Fig. 1) was obtained with 92% ee as the final product instead of the expected amino acid (Table 2, entry 3). We tried to oxidize aldehyde **9** by treating it again with the same oxidants as before, but decomposition was observed. We do not have any good explanation for the different behaviour of compound *ent*-**3gc** in the oxidation step. Finally, aliphatic imines



Scheme 4. Reagents and conditions: (i) $CH_2{=}CHCH_2MgBr$ (1.3 equiv), Me_2Zn (0.15 equiv), THF, 20 °C; (ii) NH_4Cl (aq); (iii) HCl, MeOH; (iv) PhCOCl (2 equiv), 2 M NaOH (aq) (34 equiv), CH_2Cl_2, 0–20 °C. (v) $RuCl_3 \times H_2O$ (5 mol %), $NaIO_4$ (6 equiv), $MeCN/H_2O/CCl_4$ (3:3:2), 20 °C.

Table 2
Asymmetric synthesis of β-amino acids via the diastereoselective addition of triorganozincates to *N*-(*tert*-butanesulfinyl)imines

Entry	Imine	Amine		Benzamide			β-Amino acid			
		No.[a]	Yield[b] (%)	No.[a]	Yield[c] (%)	ee[d] (%)	No.[a]	R^2	Yield[e] (%)	ee[f] (%)
1	**1a**	*ent*-**2ga**	74	*ent*-**3ga**	99	90	**8a**	Ph	91	88
2	**1b**	*ent*-**2gb**	69	*ent*-**3gb**	87	92	**8b**	4-ClC_6H_4	99	92
3	**1c**	*ent*-**2gc**	81	*ent*-**3gc**	90	94	**9**[g]	4-$MeOC_6H_4$	97	92
4	**1d**	*ent*-**2gd**	64	*ent*-**3gd**	87	70	**8d**	$Ph(CH_2)_2$	99	70
5	**1e**	*ent*-**2ge**	74	*ent*-**3ge**	80	72	**8e**	$Me(CH_2)_7$	91	72

[a] Product number corresponding to the major enantiomer.
[b] Overall isolated yield from the imine to the free amine based on the starting imine **1**.
[c] Isolated yield after column chromatography (hexane/ethyl acetate) based on the free amine *ent*-**2**. All isolated compounds were ⩾95% pure (GC and/or 300 MHz ^{1}H NMR).
[d] Determined by HPLC using a ChiralCel OD-H column. The absolute configuration of the major enantiomer was deduced by comparison of the sign of the specific rotation of the free primary amine *ent*-**2** with the reported data.
[e] Isolated yield after column chromatography (hexane/ethyl acetate/methanol) based on the benzoylated amine *ent*-**3**. All isolated compounds were ⩾95% pure (GC and/or 300 MHz ^{1}H NMR).
[f] Determined for the corresponding methyl ester by HPLC using a ChiralCel OD-H column.
[g] The oxidation step did not give the expected β-amino acid, but the corresponding intermediate aldehyde **9** (see Fig. 1).

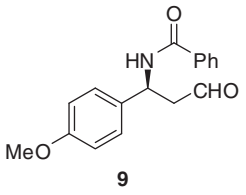


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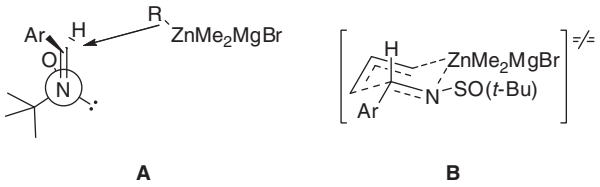
Figure 1.



A **B**

Figure 2.

1d and **1e** also led to the expected β-amino acids **8d** and **8e** in very good yields, although in lower ees than in the reactions with benzaldimines **1a–c** (Scheme 4, Table 2, entries 4 and 5). Although several examples of the synthesis of β-amino acids by oxidative cleavage of homoallylamines have been reported,[17] to the best of our knowledge this is the first time that the allylation of sulfinylimines[18] has been used as a key step for the preparation of those amino acids.

In all cases, as we had previously observed,[11] the two diastereoisomers of the sulfinamides were the only products that could be detected in the crude reaction mixtures after the addition of the triorganozincates to imines **1** or **5**. Therefore, they could be submitted to the desulfinylation procedure without further purification, affording the expected primary amines. By comparison of the sign of their specific rotations with the data reported in the literature, the absolute configuration of the amines **2**, *ent*-**2** and **6** could be determined. The oxidation of the benzamides **3** and *ent*-**3** was performed following a literature procedure.[19] The enantiomeric excesses of the N-protected amino acids **4** and *ent*-**4** were determined for their corresponding methyl esters[20] by HPLC analysis using a ChiralCel OD-H column. As it can be seen in Tables 1 and 2, in some cases there was a very slight loss of optical purity (2% maximum) during the whole process from the imines to the amino acids: the ee values of the final amino acids match very well with the ee's of the corresponding amines **2** or *ent*-**2**.

The stereochemical outcome of the addition reactions could be rationalized assuming that they occur through the transition states depicted in Figure 2. An alkyl or vinyl group would add to the imine from the less sterically hindered *Re*-face through an open transition state where the imine adopts the conformation shown in Figure 2A, which is its preferred conformation according to theoretical calculations.[21] In the case of the allylation reactions, the addition of the nucleophile could take place from the *Si*-face of the imine via a chair-like transition state like the one depicted in Figure 2B through a S_E2' mechanism. The coordination of the oxygen atom of the sulfinyl group to the magnesium atom could provide further stabilization to both transition states. Theoretical calculations are in progress in order to establish the viability of these proposals.

3. Conclusions

In conclusion, the addition of triorganozincates to *N*-(*tert*-butanesulfinyl)imines can be used as a key step in the asymmetric synthesis of α- and β-amino acids and derivatives. Using the same sulfinyl group on the nitrogen of the starting imine, the absolute configuration of the final amino acid can be controlled by an appropriate choice of the way in which the synthetic equivalent of the carboxy group is introduced. The methodology is also applicable to the synthesis of α,α-disubstituted α-amino acids with high enantiomeric purity by using α-imino esters as substrates. Further efforts to find more synthetic applications of this addition methodology are currently underway in our laboratories.

4. Experimental

4.1. General

For general experimental information, see Ref. 22. When mentioned, an R_f value measured on deactivated silica gel means that the TLC plate was eluted with a mixture of 5% triethylamine in hexane and dried before applying the sample. Unless otherwise stated, NMR samples were prepared using $CDCl_3$ as solvent. All starting materials needed for the synthesis of imines **1** and the solutions of EtMgBr (1 M in THF, Aldrich), Me_2CHCH_2MgCl (2 M in THF, Aldrich), $Me(CH_2)_4MgBr$ (2 M in Et_2O, Aldrich), $PhCH_2MgCl$ (1 M in THF, Acros), *i*-PrMgBr (2 M in THF, Aldrich), CH_2=CHMgBr (1 M in THF, Aldrich), CH_2=$CHCH_2MgBr$ (1 M in Et_2O, Aldrich) and Me_2Zn (2 M in toluene, Aldrich) were commercially available and were used as received. Optical rotations were measured on a Perkin–Elmer 341 polarimeter. HPLC analyses were performed at 25 °C on a JASCO apparatus, equipped with a PU-2089 Plus pump, a MD-2010 Plus detector and an AS-2059 Plus automatic injector.

The HRMS (EI) were performed by the Technical Services of the University of Alicante on a Finnigan MAT 95S apparatus.

4.2. Synthesis of imines 1

Imines **1** and **5** were prepared by reaction of the corresponding aldehydes or ketone with (*R*)-*tert*-butanesulfinamide, according to the literature procedures.[23] Compounds **1a**,[23a] **1b**,[24] **1c**,[24] **1d**,[25] **1e**,[11b] **1f**[26] and **5**[11b] were characterized by comparison of their physical and spectroscopic data with those reported in the literature.

4.3. Addition of triorganozincates to imines 1: General procedure

The addition of the catalytically generated organozincates to imines **1** or **5** was carried out as previously described by us.[11c] All the reactions used as the first step for the preparation of α-amino acids were performed at −78 °C (or −100 °C in the case of the synthesis of amine **6a**). The temperature of the addition reactions that led to the homoallylic amines *ent*-**2ga**–**ge** was 20 °C. In all cases, the obtained diastereomeric mixtures of sulfinamides were submitted to the desulfinylation procedure without further purification.

4.4. Desulfinylation of the addition products. Isolation of amines 2, *ent*-2 and 6: General procedure

The crude mixture of the addition reaction was dissolved in a 1.5 M solution of HCl in methanol (4 mL; prepared by dropwise addition of $SOCl_2$ to methanol at 0 °C) and stirred overnight at room temperature. Then, the solvent was evaporated, a 2 M aqueous HCl solution (5 mL) was added and the mixture was extracted with ethyl acetate (3 × 5 mL). The organic layers were discarded. The aqueous layer was basified with a buffer solution of NH_3 (1 M)/NH_4Cl (1 M) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried (Na_2SO_4). After filtration and evaporation of the solvent, pure amines **2**, *ent*-**2** and **6** were obtained in the yields indicated in Tables 1 and 2. Amines **2a**,[27] **2fa**[28] and **6a**[11b] were characterized by comparison of their physical and spectroscopic data with those reported in the literature. The corresponding physical, spectroscopic and analytical data for the other amines follow.

4.4.1. (*R*)-1-(4-Chlorophenyl)prop-2-en-1-amine 2b[29]

Colourless oil; R_f 0.15 (hexane/ethyl acetate: 4/1, deactivated silica gel); $[\alpha]_D^{20} = +6.0$ (*c* 0.2, $CHCl_3$, 92% ee); *ν* (film) 3397 (NH), 3019 (HC=C), 1216 cm^{-1} (CN); δ_H 2.35 (s, 2H, NH_2), 4.51 (d, 1H, *J* = 6.1 Hz, CHN), 5.12 (d, 1H, *J* = 10.3 Hz, 1 × C*H*H=C), 5.23 (d, 1H, *J* = 17.0 Hz, 1 × C*H*H=C), 5.91–6.02 (m, 1H, C*H*=CH_2), 7.29 (s, 4H, ArH); δ_C 57.8 (CHN), 114.1 (*C*H_2=C), 128.0 (2C), 128.6 (2C), 132.7, 142.8 (ArC), 141.8 (*C*H=CH_2); *m*/*z* 167 (M^+, 25%), 166 (80), 142 (29), 140 (100), 132 (62), 130 (31), 115 (53), 77 (36), 56 (30), 55 (30).

4.4.2. (*R*)-1-(4-Methoxyphenyl)prop-2-en-1-amine 2c

Colourless oil; R_f 0.16 (hexane/ethyl acetate: 4/1, deactivated silica gel); $[\alpha]_D^{20} = -16.0$ (*c* 0.2, $CHCl_3$, 88% ee); *ν* (film) 3361 (NH), 1609 (HC=C), 1247 (CO), 1035 cm^{-1} (CN); δ_H 1.60 (s, 2H, NH_2), 3.80 (s, 3H, Me), 4.49 (d, 1H, *J* = 6.1 Hz, CHN), 5.09 (dt, 1H, *J* = 10.2, 1.5 Hz, 1 × C*H*H=C), 5.22 (dt, 1H, *J* = 17.1, 1.5 Hz, 1 × C*H*H=C), 6.00 (ddd, *J* = 17.1, 10.2, 6.1 Hz, C*H*=CH_2), 6.87, 7.26 (2d, 2H each, *J* = 8.7 Hz each, ArH); δ_C 55.3 (Me), 57.7 (CHN), 113.4 (*C*H_2=C), 113.9 (2C), 127.7 (2C), 136.6, 155.7 (ArC), 142.5 (*C*H=CH_2); *m*/*z* 163 (M^+, 10%), 162 (14), 147 (14), 146 (100), 136 (20), 134 (11), 132 (16), 131 (61), 115 (18), 103 (67), 102 (21), 77 (28), 63 (11), 51 (10).

4.4.3. (*S*)-5-Phenylpent-1-en-3-amine 2d[30]

Colourless oil; R_f 0.28 (hexane/ethyl acetate: 1/1, deactivated silica gel); $[\alpha]_D^{20} = +4.0$ (*c* 0.5, $CHCl_3$, 60% ee); *ν* (film) 3092, 3072, 1609, 1449 (HC=C), 1261 cm^{-1} (CN); δ_H 1.35 (br s, 2H, NH_2), 1.75 (dt, 2H, *J* = 8.4, 7.4 Hz, CH_2CH_2CH), 2.67 (dd, 2H, *J* = 8.4, 7.4 Hz, CH_2Ph), 3.32 (qt, 1H, *J* = 6.7, 0.9 Hz, CHN), 5.06 (ddd, 1H, *J* = 10.3, 1.4, 1.1 Hz, 1 × C*H*H=C), 5.14 (dt, 1H, *J* = 17.2, 1.1 Hz, 1 × C*H*H=C), 5.82 (ddd, 1H, *J* = 17.2, 10.3, 6.8 Hz, C*H*=CH_2), 7.18–7.30 (m, 5H, ArH); δ_C 32.4 (CH_2Ph), 39.1 (CH_2CH_2CH), 54.0 (CHN), 113.8 (*C*H_2=C), 125.7, 128.3 (2C), 128.4 (2C), 142.1 (ArC), 143.2 (*C*H=CH_2); *m*/*z* 161 (M^+, 2%), 144 (21), 142 (12), 141 (11), 129 (20), 128 (11), 115 (12), 105 (11), 104 (39), 103 (20), 91 (30), 78 (17), 77 (17), 56 (100), 51 (16).

4.4.4. (*S*)-Undec-1-en-3-amine 2e

Colourless oil; R_f 0.20 (hexane/ethyl acetate: 1/1, deactivated silica gel); $[\alpha]_D^{20} = +9.2$ (*c* 1, $CHCl_3$, 60% ee); *ν* (film) 3024 (HC=C), 1244 cm^{-1} (CN); δ_H 0.88 (t, 3H, *J* = 6.7 Hz, Me), 1.22–1.44 [m, 14H, $(CH_2)_7$], 3.27 (qd, 1H, *J* = 6.7, 1.1 Hz, CHN), 5.00 (ddd, 1H, *J* = 10.3, 1.5, 1.1 Hz, 1 × C*H*H=C), 5.09 (ddd, 1H, *J* = 17.2, 1.5, 1.1 Hz, 1 × C*H*H=C), 5.78 (ddd, 1H, *J* = 17.2, 10.3, 6.7 Hz, C*H*=CH_2); δ_C 14.1 (Me), 22.6, 26.1, 29.3, 29.5, 29.6, 31.9, 37.6 [$(CH_2)_7$], 54.5 (CHN), 113.1 (*C*H_2=C), 143.6 (*C*H=CH_2); HRMS: $M^+ - C_2H_3$ found 142.1633, $C_9H_{20}N$ requires 142.1596.

4.4.5. (*R*)-1-(2-Furyl)-3-methylbutan-1-amine 2fb[31]

Yellow oil; R_f 0.22 (hexane/ethyl acetate: 1/1, deactivated silica gel); $[\alpha]_D^{20} = +46.0$ (*c* 1, $CHCl_3$, 96% ee); *ν* (film) 3386 (NH), 1649, 1555, 1461 (HC=C), 1142 cm^{-1} (CN); δ_H 0.90, 0.92 (2d, 3H each, *J* = 6.2 Hz each, Me_2CH), 1.52–1.70 (m, 3H, C*H*Me_2 and CH_2), 1.40 (br s, 2H, NH_2), 3.98 (t, 1H, *J* = 7.0 Hz, CHN), 6.11 (d, 1H, *J* = 3.2 Hz, O–C=CH), 6.29 (dd, 1H, *J* = 3.2, 1.8 Hz, O–CH=C*H*), 7.33 (dd, 1H, *J* = 1.8, 0.8 Hz, O–CH); δ_C 22.3, 22.8 (2 × Me), 24.9 (*C*HMe), 45.3 (CH_2), 47.8 (CHN), 104.2 (O–C=C*C*H), 110.0 (O–CH=*C*H), 141.2 (O–CH), 159.0 (O–C); *m*/*z* 153 (M^+, <1%), 136 (14), 121 (20), 96 (100), 91 (10).

4.4.6. (*R*)-1-(2-Furyl)hexan-1-amine 2fc

Colourless oil; R_f 0.29 (ethyl acetate, deactivated silica gel); $[\alpha]_D^{20} = +10.4$ (*c* 1, $CHCl_3$, 92% ee); *ν* (film) 3324 (NH), 1645, 1469 (HC=C), 1142 cm^{-1} (CN); δ_H 0.80 (d, 3H, *J* = 6.7 Hz, Me), 1.16–1.36 [m, 6H, $(CH_2)_3$Me], 1.53–1.77 (m, 2H, CH_2CH), 1.82 (br s, 2H, NH_2), 3.03 (t, 1H, *J* = 6.9 Hz, CHN), 6.04 (d, 1H, *J* = 3.2 Hz, O–C=CH), 6.23 (dd, 1H, *J* = 3.2, 1.8 Hz, O–CH=C*H*), 7.26 (dd, 1H, *J* = 1.8, 0.8 Hz, O–CH); δ_C 14.0 (Me), 22.5, 25.8, 31.7, 36.2 [$(CH_2)_4$], 49.8 (CHN), 104.2 (O–C=CH), 109.9 (O–CH=*C*H), 141.2 (O–CH), 159.0 (O–C); *m*/*z* 167 (M^+, <1%), 150 (19), 107 (36), 96 (100), 94 (35), 79 (22), 77 (18).

4.4.7. (*R*)-1-(2-Furyl)-2-phenylethanamine 2fd[32]

Orange oil; R_f 0.24 (ethyl acetate, deactivated silica gel); $[\alpha]_D^{20} = -10.5$ (*c* 1, EtOH, 94% ee); *ν* (film) 3385 (NH), 3078, 3024, 1602, 1495, 1455 (HC=C), 1155 cm^{-1} (CN); δ_H 2.07 (br s, 2H, NH_2), 2.90 (dd, 1H, *J* = 13.4, 8.3 Hz, 1 × C*H*H), 3.17 (dd, 1H, *J* = 13.4, 5.3 Hz, 1 × C*H*H), 4.21 (dd, 1H, *J* = 8.3, 5.3 Hz, CHN), 6.10 (d, 1H, *J* = 3.2 Hz, O–C=CH), 6.30 (dd, 1H, *J* = 3.2, 1.8 Hz, O–CH=C*H*), 7.11–7.33 (m, 5H, ArH), 7.37 (dd, 1H, *J* = 1.8, 0.7 Hz, O–CH); δ_C 42.9 (CH_2), 51.1 (CHN), 104.9 (O–C=*C*H), 110.0 (O–CH=*C*H), 126.5, 128.4 (2C), 129.3 (2C), 138.1 (ArC), 141.3 (O–CH), 157.8 (O–C); *m*/*z* 187 (M^+, <1%), 170 (99), 169 (38), 142 (20), 141 (97), 115 (48), 96 (100), 91 (13).

4.4.8. (*R*)-1-(2-Furyl)-2-methylpropan-1-amine 2fe[28]

Colourless oil; R_f 0.18 (ethyl acetate, deactivated silica gel); $[\alpha]_D^{20} = +6.4$ (*c* 0.6, $CHCl_3$, 95% ee); *v* (film) 3113 (NH), 1644, 1594, 1465 (HC=C), 1148 cm^{-1} (CN); δ_H 0.87 0.94 (2d, 3H each, *J* = 6.8 Hz each, Me_2CH), 1.64 (br s, 2H, NH_2), 2.00 (oct, 1H, *J* = 6.8 Hz, $CHMe_2$), 3.69 (d, 1H, *J* = 6.2 Hz, CHN), 6.12 (d, 1H, *J* = 3.2 Hz, O–C=CH), 6.30 (dd, 1H, *J* = 3.2, 1.8 Hz, O–CH=CH), 7.33 (d, 1H, *J* = 1.8 Hz, O–CH); δ_C 18.3, 19.2 (Me_2CH), 33.4 ($CHMe_2$), 55.8 (CHN), 105.0 (O–C=CH), 109.8 (O–CH=CH), 141.0 (O–CH), 158.3 (O–C); *m*/*z* 122 (100), 109 (67), 104 (12).

4.4.9. (*S*)-1-Phenylbut-3-en-1-amine *ent*-2ga[18a]

Yellow oil; R_f 0.50 (hexane/ethyl acetate: 1/1, deactivated silica gel); $[\alpha]_D^{20} = -25.3$ (*c* 1, $CHCl_3$, 90% ee); *v* (film) 3379 (NH), 3065, 3026, 1639, 1492 cm^{-1} (HC=C); δ_H 1.70 (br s, 2H, NH_2), 2.29–2.50 (m, 2H, CH_2CN), 3.97 (dd, 1H, *J* = 8.1, 5.3 Hz, CHN), 5.06 (d, 1H, *J* = 10.2 Hz, 1 × *CH*H=C), 5.12 (d, 1H, *J* = 17.1 Hz, 1 × *CH*H=C), 5.74 (dddd, 1H, *J* = 17.2, 10.3, 8.1, 6.3 Hz, *CH*=CH_2), 7.20–7.32 (m, 5H, ArH); δ_C 44.1 (CH_2CN), 55.2 (CHN), 117.5 (CH_2=C), 126.2 (2C), 126.8, 128.3 (2C), 145.7 (2C) (ArC), 135.3 (*CH*=CH_2); *m*/*z* 106 ($M^+-C_3H_5$, 100%), 79 (27), 77 (20).

4.4.10. (*S*)-1-(4-Chlorophenyl)but-3-en-1-amine *ent*-2gb[33]

Colourless oil; R_f 0.29 (ethyl acetate, deactivated silica gel); $[\alpha]_D^{20} = -44.7$ (*c* 1, $CHCl_3$, 92% ee); *v* (film) 3375 (NH), 3076, 1640 (HC=C), 1091 cm^{-1} (CN); δ_H 1.54 (br s, 2H, NH_2), 2.32 (ddt, 1H, *J* = 13.7, 7.9, 0.9 Hz, 1 × *CH*HCN), 2.42 (ddt, 1H, *J* = 13.7, 5.6, 1.2 Hz, 1 × *CH*HCN), 3.99 (dd, 1H, *J* = 7.9, 5.6 Hz, CHN), 5.09 (dq, 1H, *J* = 10.3, 1.0 Hz, 1 × *CH*H=CH), 5.11 (dq, 1H, *J* = 17.0, 1.6 Hz, 1 × *CH*H=CH), 5.72 (dddd, 1H, *J* = 17.0, 10.3, 7.9, 6.5 Hz, *CH*=CH_2), 7.29 (s, 4H, 2 × ArH); δ_C 44.2 (CH_2CN), 54.7 (CHN), 118.0 (CH_2=C), 127.7 (2C), 128.4 (2C), 132.5, 144.2 (ArC), 135.0 (*CH*=CH_2); *m*/*z* 181 (M^+, <1%), 142 (32), 140 (100), 77 (16).

4.4.11. (*S*)-1-(4-Methoxyphenyl)but-3-en-1-amine *ent*-2gc[34]

Yellow oil; R_f 0.36 (hexane/ethyl acetate: 1/1, deactivated silica gel); $[\alpha]_D^{20} = -37.5$ (*c* 0.55, $CHCl_3$, 94% ee); *v* (film) 3321 (NH), 3069, 1609 (HC=C), 1250 (CO), 1178 cm^{-1} (CN); δ_H 2.34 (dtdd, 1H, *J* = 13.8, 8.0, 1.5, 1.0 Hz, 1 × *CH*HCN), 2.43 (ddddd, 1H, *J* = 13.8, 6.4, 5.4, 1.5, 1.0 Hz, 1 × *CH*HCN), 3.80 (s, 3H, MeO), 3.95 (dd, 1H, *J* = 8.0, 5.4 Hz, CHN), 5.07 (ddt, 1H, *J* = 10.2, 2.0, 1.0 Hz, 1 × *CH*H=CH), 5.11 (ddt, 1H, *J* = 17.1, 2.0, 1.5 Hz, 1 × *CH*H=CH), 5.74 (dddd, 1H, *J* = 17.1, 10.2, 8.0, 6.4 Hz, *CH*=CH_2), 6.87, 7.26 (2d, 2H each, *J* = 8.5 Hz each, ArC); δ_C 44.2 (CH_2CN), 54.7 (CHN), 55.2 (Me), 117.5 (CH_2=C), 113.7 (2C), 127.3 (2C), 137.9, 158.5 (ArC), 135.6 (*CH*=CH_2); *m*/*z* 177 (M^+, 13%), 176 (100), 161 (13), 146 (7), 91 (7), 77 (5).

4.4.12. (*R*)-1-Phenylhex-5-en-3-amine *ent*-2gd[34]

Yellow oil; R_f 0.54 (hexane/ethyl acetate: 1/1, deactivated silica gel); $[\alpha]_D^{20} = +6.9$ (*c* 0.7, $CHCl_3$, 70% ee); *v* (film) 3058, 3027, 1640, 1599, 1495, 1448 (HC=C), 1381 cm^{-1} (CN); δ_H 1.37 (s, 2H, NH_2), 1.61 (dddd, 1H, *J* = 13.6, 10.1, 7.9, 5.7 Hz, 1 × CHC*H*HCH$_2$), 1.76 (dddd, 1H, *J* = 13.6, 10.2, 6.2, 4.7 Hz, 1 × CHC*H*HCH$_2$), 2.03 (dtt, 1H, *J* = 13.7, 7.9, 1.0 Hz, 1 × *CH*HCH=CH_2), 2.27 (dddt, 1H, *J* = 13.7, 6.3, 1.4 Hz, 1 × *CH*HCH=CH_2), 2.64 (ddd, 1H, *J* = 13.7, 10.1, 6.2 Hz, 1 × *CH*HPh), 2.76 (ddd, 1H, *J* = 13.7, 10.2, 5.7 Hz, 1 × *CH*HPh), 2.82 (tt, 1H, *J* = 7.9, 4.7 Hz, CHN), 5.09 (ddt, 1H, *J* = 10.7, 2.0, 1.0 Hz, 1 × *CH*H=CH), 5.10 (ddt, 1H, *J* = 16.3, 2.0, 1.4 Hz, 1 × *CH*H=CH), 5.79 (dddd, 1H, *J* = 16.3, 10.7, 8.1, 6.3 Hz, *CH*=CH_2), 7.30–7.16 (m, 5H, ArH); δ_C 32.6 (CH_2Ph), 39.4 ($CHCH_2CH_2$), 42.6 (CH_2CH=CH_2), 50.1 (CHN), 117.5 (CH_2=C), 125.7, 128.31 (2C), 128.34 (2C), 142.2 (ArC), 135.6 (*CH*=CH_2); *m*/*z* 134 ($M^+-C_3H_5$, 2%), 134 (81), 117 (24), 91 (100), 70 (16).

4.4.13. (*R*)-Dodec-1-en-4-amine *ent*-2ge[35]

Colourless oil; R_f 0.24 (ethyl acetate, deactivated silica gel); $[\alpha]_D^{20} = -4.0$ (*c* 0.5, $CHCl_3$, 72% ee); *v* (film) 1636, 1459 (HC=C), 1258 cm^{-1} (CN); δ_H 0.88 (t, 3H, *J* = 6.6 Hz, Me), 1.22–1.32 [m, 12H, $(CH_2)_6$Me], 1.97 (dtt, 1H, *J* = 13.7, 8.0, 0.9 Hz, 1 × *CH*HCH=CH_2), 2.24 (dddt, *J* = 13.7, 6.2, 4.6, 1.3 Hz, 1 × *CH*HCH=CH_2), 2.73–2.82 (m, 1H, CHN), 5.08 (d, 1H, *J* = 16.1 Hz, 1 × *CH*H=CH), 5.09 (d, 1H, *J* = 16.1 Hz, 1 × *CH*H=CH), 5.72–5.86 (m, 1H, *CH*=CH_2); δ_C 14.1 (Me), 22.7, 26.3, 29.3, 29.6, 29.8, 31.9, 40.5, 42.5 (8 × CH_2), 50.6 (CHN), 117.3 (CH_2=C), 136.0 (*CH*=CH_2); *m*/*z* 167 (32), 150 (12), 149 (100), 71 (11), 70 (13), 57 (16).

4.4.14. (*R*)-Ethyl 2-amino-2,3-diphenylpropanoate 6b[36]

Yellow oil; R_f 0.47 (hexane/ethyl acetate: 1/1, deactivated silica gel); $[\alpha]_D^{20} = +7.6$ (*c* 0.5, $CHCl_3$, 80% ee); *v* (film) 3386 (NH), 3061, 3029 (HC=C), 1728 (C=O), 1195 cm^{-1} (CN); δ_H 1.24 (t, 3H, *J* = 7.1 Hz, Me), 2.37 (br s, 2H, NH_2), 3.18, 3.64 (2d, 1H each, *J* = 13.3 Hz each, CH_2Ph), 4.19 (q, 1H, *J* = 7.1 Hz, CH_2O), 7.11–7.60 (m, 10H, ArH); δ_C 14.0 (Me), 45.7 (CH_2Ph), 61.6 (CH_2O), 64.4 (CN), 125.6 (2C), 127.0 (2C), 127.6, 128.2 (2C), 128.3, 130.5 (2C), 136.0, 142.6 (ArC), 174.7 (C=O); *m*/*z* 240 ($M^+-C_2H_5$, <1%), 197 (14), 196 (88), 179 (16), 178 (100), 150 (11), 104 (56), 91 (15), 71 (10).

4.4.15. (*R*)-Ethyl 2-amino-3-methyl-2-phenylbutanoate 6c

Yellow oil; R_f 0.42 (hexane/ethyl acetate: 1/1, deactivated silica gel); $[\alpha]_D^{20} = -12.1$ (*c* 0.5, $CHCl_3$, 62% ee); *v* (film) 3400 (NH), 1726 (C=O), 1218 cm^{-1} (CN); δ_H 0.67, 1.01 (2d, 3H each, *J* = 6.8 Hz each, Me_2CH), 1.23 (t, 3H, *J* = 7.1 Hz, $MeCH_2$), 1.93 (br s, 2H, NH_2), 2.76 (septet, 1H, *J* = 6.8 Hz, $CHMe_2$), 4.15 (qd, 2H, *J* = 7.1, 0.9 Hz, CH_2), 7.22–7.66 (m, 5H, ArH); δ_C 14.0 ($MeCH_2$), 16.2, 17.9 (Me_2CH), 35.3 (*CH*Me), 61.3 (CH_2), 66.9 (CN), 125.9 (2C), 127.1, 128.1 (2C), 142.2 (ArC), 175.3 (C=O); *m*/*z* 221 (M^+, <1%), 178 (49), 149 (12), 148 (100), 104 (39); HRMS: $M^+-C_3H_7$ found 178.0886, $C_{10}H_{12}NO_2$ requires 178.0868.

4.5. Benzoylation of the free amines. Isolation of compounds 3, *ent*-3 and 7: General procedure

An aqueous 2 M NaOH solution (10 mL) was added to a solution of the corresponding amine (0.57 mmol) in CH_2Cl_2 (10 mL) at 0 °C and the mixture was stirred for 5 min. Benzoyl chloride (1.14 mmol) was added and the mixture was stirred overnight at room temperature. Then, water (5 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried (Na_2SO_4). After filtration and evaporation of the solvent, the pure benzamides **3**, *ent*-**3** and **7** were obtained. These benzamides were analyzed by HPLC on a ChiralCel OD-H column using a 254 nm UV detector, 10% *i*-PrOH in hexane as eluent and a flow rate of 0.5 mL/min. The retention times were 18.5 (**3a**), 29.7 (*ent*-**3a**), 26.0 (**3b**), 38.3 (*ent*-**3b**), 33.9 (**3c**), 40.7 (*ent*-**3c**), 35.0 (**3d**), 43.2 (*ent*-**3d**), 15.3 (*ent*-**3e**), 19.3 (**3e**), 15.8 (**3fa**), 19.2 (*ent*-**3fa**), 12.8 (**3fb**), 16.1 (*ent*-**3fb**), 13.2 (**3fc**), 18.9 (*ent*-**3fc**), 27.6 (**3fd**), 33.0 (*ent*-**3fd**), 14.4 (**3fe**), 15.7 (*ent*-**3fe**), 22.5 (**3ga**), 37.5 (*ent*-**3ga**), 23.8 (**3gb**), 31.7 (*ent*-**3gb**), 33.2 (**3gc**), 38.5 (*ent*-**3gc**), 34.1 (**3gd**), 43.5 (*ent*-**3gd**), 14.1 (*ent*-**3ge**), 19.2 (**3ge**), 13.3 (*ent*-**7a**; 5% *i*-PrOH in hexane as eluent), 15.4 (**7a**; 5% *i*-PrOH in hexane as eluent), 33.3 (*ent*-**7b**; 2% *i*-PrOH in hexane as eluent), 35.6 (**7b**; 2% *i*-PrOH in hexane as eluent), 61.0 (*ent*-**7c**; 1% *i*-PrOH in hexane as eluent), 71.0 (**7c**; 1% *i*-PrOH in hexane as eluent). The yields and enantiomeric excesses obtained are collected in Tables 1 and 2. Benzamides **3a**,[29] **3fa**,[28] **3fe**,[28] *ent*-**3ga**[37] were characterized by comparison of their physical and spectroscopic data with those reported in the

literature. The corresponding physical, spectroscopic and analytical data for the other benzamides follow.

4.5.1. (*R*)-*N*-[1-(4-Chlorophenyl)allyl]benzamide 3b[14]

Yellow oil; R_f 0.16 (hexane/ethyl acetate: 4/1); $[\alpha]_D^{20} = +36.0$ (*c* 1, $CHCl_3$, 92% ee); *v* (film) 3295 (NH), 3091, 3058 (HC=C), 1636 (C=O), 1528 (N–C=O), 1342 cm^{-1} (CN); δ_H 5.30 (ddd, 1H, *J* = 17.0, 1.7, 0.9 Hz, 1 × C*H*H=C), 5.34 (ddd, 1H, *J* = 10.4, 1.5, 0.9 Hz, 1 × C*H*H=C), 5.82 (dd, 1H, *J* = 8.0, 5.5 Hz, CHN), 6.09 (ddd, 1H, *J* = 17.0, 10.4, 5.5 Hz, C*H*=CH_2), 6.36 (d, 1H, *J* = 8.0 Hz, NH), 7.29–7.54 (m, 9H, ArH); δ_C 54.9 (CHN), 116.9 (*C*H_2=C), 126.9 (2C), 128.7 (4C), 128.9 (2C), 131.7, 133.6, 134.1, 139.0 (ArC), 136.7 (*C*H=CH_2), 160.5 (C=O); *m*/*z* 271 (M^+, 11%), 256 (14), 115 (38), 105 (100), 77 (48), 51 (15).

4.5.2. (*R*)-*N*-[1-(4-Methoxyphenyl)allyl]benzamide 3c[14]

Colourless oil; R_f 0.14 (hexane/ethyl acetate: 4/1); $[\alpha]_D^{20} = +43.6$ (*c* 1, $CHCl_3$, 88% ee); *v* (film) 3314 (NH), 3078, 3052, 1628 (C=O), 1525 (N–C=O), 1249 (CO), 1238 cm^{-1} (CN); δ_H 3.80 (s, 3H, Me), 5.29 (ddd, 1H, *J* = 17.4, 1.7, 1.1 Hz, 1 × C*H*H=C), 5.30 (ddd, 1H, *J* = 10.2, 1.7, 1.1 Hz, 1 × C*H*H=C), 5.80 (ddt, 1H, *J* = 8.1, 5.1, 1.7 Hz, CHN), 6.10 (ddd, 1H, *J* = 17.4, 10.2, 5.1 Hz, C*H*=CH_2), 6.33 (d, 1H, *J* = 8.1 Hz, NH), 6.90, 7.30 (2d, 2H each, *J* = 8.7 Hz each, 4 × ArH), 7.42, 7.49, 7.79 (t, t and d, respectively, 2H, 1H and 2H, respectively, *J* = 7.3 Hz each, 5 × ArH); δ_C 54.9 (Me), 55.3 (CHN), 115.8 (*C*H_2=C), 114.2 (2C), 128.6 (2C), 134.4, 159.2 (ArC), 137.3 (*C*H=CH_2), 166.4 (C=O); *m*/*z* 267 (M^+, 23%), 252 (25), 162 (16), 146 (58), 131 (44), 121 (24), 105 (100), 103 (76), 77 (92), 63 (15), 51 (36).

4.5.3. (*S*)-*N*-[1-(2-Phenylethyl)prop-2-enyl]benzamide 3d[38]

Colourless oil; R_f 0.36 (hexane/ethyl acetate: 4/1); $[\alpha]_D^{20} = +9.7$ (*c* 0.7, $CHCl_3$, 60% ee); *v* (film) 3300 (NH), 3026 (HC=C), 1634 (C=O), 1537 (N–C=O), 1294 cm^{-1} (CN); δ_H 1.97 (dq, 1H, *J* = 13.9, 7.6 Hz, 1 × C*H*HCH_2Ph), 2.02 (dq, 1H, *J* = 13.9, 7.8 Hz, 1 × C*H*HCH_2Ph), 2.74 (t, 2H, *J* = 7.8 Hz, CH_2Ph), 4.76 (q, 1H, *J* = 6.9 Hz, CHN), 5.19 (dt, 1H, *J* = 10.4, 1.3 Hz, 1 × C*H*H=C), 5.24 (dt, 1H, *J* = 17.2, 1.3 Hz, 1 × C*H*H=C), 5.90 (ddd, 1H, *J* = 17.2, 10.4, 5.5 Hz, C*H*=CH_2), 6.05 (d, 1H, *J* = 7.4 Hz, NH), 7.12–7.69 (m, 10H, ArH); δ_C 32.2 (CH_2Ph), 36.3 (*C*$H_2$$CH_2$Ph), 51.6 (CHN), 115.4 (*C*H_2=C), 126.0, 126.8 (2C), 128.4 (2C), 128.50 (2C), 128.55 (2C), 131.4, 134.5, 141.5 (ArC), 138.0 (*C*H=CH_2), 166.7 (C=O); *m*/*z* 265 (M^+, 2%), 161 (51), 105 (100), 77 (30).

4.5.4. (*S*)-*N*-(1-Octylprop-2-enyl)benzamide 3e

White solid; mp 65–66 °C; R_f 0.56 (hexane/ethyl acetate: 4/1); $[\alpha]_D^{20} = +11.0$ (*c* 0.4, $CHCl_3$, 60% ee); *v* (film) 3383 (NH), 1634 (C=O), 1539 (N–C=O), 1114 cm^{-1} (CN); δ_H 0.87 (t, 3H, *J* = 6.8 Hz, Me), 1.17–1.45 [m, 12H, (CH_2)$_6$Me], 1.62 (dt, 1H, *J* = 14.6, 6.8 Hz, 1 × C*H*HCN), 1.64 (dt, 1H, *J* = 14.6, 6.7 Hz, 1 × C*H*HCN), 4.66 (quintet, 1H, *J* = 7.0 Hz, CHN), 5.14 (d, 1H, *J* = 10.4 Hz, 1 × C*H*H=C), 5.23 (d, 1H, *J* = 17.2 Hz, 1 × C*H*H=C), 5.86 (ddd, 1H, *J* = 17.2, 10.4, 5.6 Hz, C*H*=CH_2), 6.04 (d, 1H, *J* = 7.9 Hz, NH), 7.40–7.81 (m, 5H, ArH); δ_C 14.1 (Me), 22.6, 25.8, 29.2, 29.42, 29.45, 31.8, 35.0 [(CH_2)$_7$], 51.7 (CHN), 114.9 (*C*H_2=C), 126.8 (2C), 128.5 (2C), 131.4, 134.7, 138.4 (*C*H=CH_2), 166.8 (C=O); *m*/*z* 273 (M^+, <2%), 161 (15), 160 (48), 105 (100), 77 (23); HRMS: M^+ found 273.2057, $C_{18}H_{27}NO$ requires 273.2093.

4.5.5. (*R*)-*N*-[1-(2-Furyl)-3-methylbutyl]benzamide 3fb[31]

White solid; mp 89–90 °C; R_f 0.50 (hexane/ethyl acetate: 3/1); $[\alpha]_D^{20} = +68.0$ (*c* 1, $CHCl_3$, 96% ee); *v* (film) 3313 (NH), 3112, 3062, 3031 (HC=C), 1631 (C=O), 1539 (N–C=O), 1292 cm^{-1} (CN); δ_H 0.96, 0.98 (2d, 3H each, *J* = 5.8 Hz each, *Me*$_2$CH), 1.60 (non, 1H, *J* = 6.7 Hz, C*H*Me), 1.79 (ddd, 1H, *J* = 13.5, 7.9, 6.6 Hz, 1 × C*H*H), 1.82 (dt, 1H, *J* = 13.5, 7.4 Hz, 1 × C*H*H), 5.41 (q, 1H, *J* = 7.9 Hz, CHN), 6.25 (d, 1H, *J* = 3.2 Hz, O–C=CH), 6.32 (dd, 1H, *J* = 3.2, 1.8 Hz, O–CH=C*H*), 7.36 (dd, 1H, *J* = 1.8, 0.7 Hz, O–CH), 7.42, 7.50, 7.78 (t, t and d, respectively, 2H, 1H and 2H, respectively, *J* = 7.2 Hz each, ArH); δ_C 22.49, 22.51 (*Me*$_2$CH), 25.0 (*C*HMe), 43.1 (CH_2), 46.0 (CHN), 106.3 (O–C=*C*H), 110.0 (O–CH=*C*H), 126.9 (2C), 128.4 (2C), 130.2, 134.4 (ArC), 141.8 (O–CH), 154.6 (O–C), 166.5 (C=O); *m*/*z* 257 (M^+, 15%), 200 (31), 136 (13), 121 (20), 105 (100), 77 (34).

4.5.6. (*R*)-*N*-[1-(2-Furyl)hexyl]benzamide 3fc[14]

White solid; mp 65–66 °C; R_f 0.52 (hexane/ethyl acetate: 3/1); $[\alpha]_D^{20} = +35.0$ (*c* 1, $CHCl_3$, 92% ee); *v* (film) 3343 (NH), 1688 (HC=C), 1633 (C=O), 1525 (N–C=O), 1291 cm^{-1} (CN); δ_H 0.87 (t, 3H, *J* = 7.0 Hz, Me), 1.26–1.41 [m, 6H, (CH_2)$_3$Me], 1.84–1.98 (m, 2H, CH_2CN), 5.32 (dt, 1H, *J* = 8.4, 7.4 Hz, CHN), 6.24 (d, 1H, *J* = 3.3 Hz, O–C=CH), 6.32 (dd, 1H, *J* = 3.3, 1.9 Hz, O–CH=C*H*), 6.38 (d, 1H, *J* = 8.4 Hz, NH), 7.36 (dd, 1H, *J* = 1.9, 0.8 Hz, O–CH), 7.40–7.80 (m, 5H, ArH); δ_C 14.0 (Me), 22.5, 25.6, 31.4, 34.1 [(CH_2)$_4$], 47.6 (CHN), 106.4 (O–C=*C*H), 110.2 (O–CH=*C*H), 126.9 (2C), 128.5 (2C), 131.5, 134.4 (ArC), 141.8 (O–CH), 154.3 (O–C), 166.6 (C=O); *m*/*z* 271 (M^+, 12%), 200 (43), 105 (100), 94 (12), 77 (33).

4.5.7. (*R*)-*N*-[1-(2-Furyl)-2-phenylethyl]benzamide 3fd[28]

Colourless oil; R_f 0.21 (hexane/ethyl acetate: 3/1); $[\alpha]_D^{20} = +1.7$ (*c* 1, $CHCl_3$, 94% ee); *v* (film) 3225 (NH), 3063 (HC=C), 1640 (C=O), 1526 (N–C=O), 1155 cm^{-1} (CN); δ_H 3.23 (dd, 1H, *J* = 13.5, 7.5 Hz, 1 × C*H*H), 3.29 (dd, 1H, *J* = 13.5, 6.2 Hz, 1 × C*H*H), 5.58 (ddd, 1H, *J* = 8.3, 7.5, 6.2 Hz, CHN), 6.08 (d, 1H, *J* = 3.2 Hz, O–C=CH), 6.28 (dd, 1H, *J* = 3.2, 1.8 Hz, O–CH=C*H*), 6.44 (d, 1H, *J* = 8.3 Hz, NH), 7.06–7.29 (m, 5H, 5 × ArH), 7.39 (dd, 1H, *J* = 1.8, 0.8 Hz, O–CH), 7.40–7.73 (m, 5H, 5 × ArH); δ_C 40.2 (CH_2), 48.9 (CHN), 107.0 (O–C=*C*H), 110.3 (O–CH=*C*H), 126.7, 126.9 (2C), 128.3 (2C), 128.6 (2C), 129.3 (2C), 131.6, 134.3, 136.9 (ArC), 141.8 (O–CH), 153.1 (O–C), 166.5 (C=O); *m*/*z* 291 (M^+, <1%), 200 (73), 105 (100), 77 (28).

4.5.8. (*S*)-*N*-[1-(4-Chlorophenyl)but-3-enyl]benzamide *ent*-3gb

White solid; mp 142–143 °C; R_f 0.36 (hexane/ethyl acetate: 4/1); $[\alpha]_D^{20} = -21.5$ (*c* 0.4, $CHCl_3$, 92% ee); *v* (film) 3222 (NH), 3018 (HC=C), 1641 (C=O), 1515 (N–C=O), 1216 cm^{-1} (CN); δ_H 2.66 (t, 2H, *J* = 7.0 Hz, CH_2), 5.16 (dd, 1H, *J* = 10.1, 1.5 Hz, 1 × C*H*H=C), 5.20 (dd, 1H, *J* = 17.1, 1.5 Hz, 1 × C*H*H=C), 5.24 (q, 1H, *J* = 7.0 Hz, CHN), 5.74 (ddt, 1H, *J* = 17.1, 10.1, 7.0 Hz, C*H*=CH_2), 6.43 (d, 1H, *J* = 7.0 Hz, NH), 7.27, 7.32 (2d, 2H each, *J* = 8.8 Hz each, 4 × ArH), 7.44–7.76 (m, 5H, 5 × ArH); δ_C 40.5 (CH_2CN), 52.1 (CHN), 118.8 (CH_2=C), 126.9 (2C), 127.8 (2C), 128.6 (2C), 128.7 (2C), 131.6, 133.0, 134.2, 140.2 (ArC), 133.6 (*C*H=CH_2), 166.7 (C=O); *m*/*z* 285 (M^+, <2%), 246 (12), 244 (34), 105 (100), 77 (29); HRMS: $M^+-C_3H_5$, found 244.0544, $C_{14}H_{11}ClNO$ requires 244.0529.

4.5.9. (*S*)-*N*-[1-(4-Methoxyphenyl)but-3-enyl]benzamide *ent*-3gc[39]

White solid; mp 150–151 °C; R_f 0.32 (hexane/ethyl acetate: 3/1); $[\alpha]_D^{20} = -25.2$ (*c* 0.8, $CHCl_3$, 94% ee); *v* (film) 3342 (NH), 3004 (HC=C), 1632 (C=O), 1532 (N–C=O), 1290 (CN), 1249 cm^{-1} (CO); δ_H 2.68 (tt, 2H, *J* = 7.0, 1.2 Hz, CH_2CN), 3.79 (s, 3H, Me), 5.11 (ddt, 1H, *J* = 10.1, 1.8, 1.2 Hz, 1 × C*H*H=C), 5.17 (ddt, 1H, *J* = 17.1, 1.8, 1.2 Hz, 1 × C*H*H=C), 5.24 (q, 1H, *J* = 7.0 Hz, CHN), 5.77 (ddt, 1H, *J* = 17.1, 10.1, 7.0 Hz, C*H*=CH_2), 6.88, 7.27 (2d, 2H each, *J* = 8.8 Hz each, 4 × ArH), 7.42, 7.49, 7.76 (t, t and d, respectively, 2H, 1H and 2H, respectively, *J* = 7.2 Hz each, 5 × ArH); δ_C 40.5 (CH_2CN), 52.2 (Me), 55.3 (CHN), 114.0 (2C), 126.9 (2C), 127.6 (2C), 128.6 (2C), 131.5, 133.7, 134.6, 158.8 (ArC), 118.3 (CH_2=C), 134.2 (*C*H=CH_2), 166.6 (C=O); *m*/*z* 281 (M^+, <1%), 240 (55), 160 (24), 159 (18), 144 (14), 129 (12), 115 (16), 105 (100), 77 (38).

4.5.10. (*R*)-*N*-[1-(2-Phenylethyl)but-3-enyl]benzamide *ent*-3gd[39]

White solid; mp 81–82 °C; R_f 0.41 (hexane/ethyl acetate: 3/1); $[\alpha]_D^{20} = -4.5$ (*c* 1, $CHCl_3$, 70% ee); *v* (film) 3310 (NH), 1682 (HC=C), 1634 (C=O), 1535 (N–C=O), 1283 cm^{-1} (CN); δ_H 1.78–2.00 (m, 2H, CH_2CH_2Ph), 2.34 (dd, 1H, *J* = 14.1, 7.2 Hz, 1 × *CH*HCH=CH_2), 2.42 (dd, 1H, *J* = 14.1, 7.2 Hz, 1 × *CH*HCH=CH_2), 2.72 (t, 2H, *J* = 8.0 Hz, CH_2Ph), 4.30 (ddt, 1H, *J* = 14.4, 8.6, 5.9 Hz, CHN), 5.11 (d, 1H, *J* = 10.2 Hz, 1 × *CH*H=C), 5.12 (d, *J* = 16.7 Hz, 1 × *CH*H=C), 5.83 (ddt, 1H, *J* = 16.7, 10.2, 7.2 Hz, *CH*=CH_2), 6.03 (br s, 1H, NH), 7.16–7.71 (m, 10H, ArH); δ_C 32.5 (CH_2Ph), 36.1 (CH_2CH_2Ph), 39.2 (CH_2CH=CH_2), 48.9 (CHN), 118.2 (CH_2=C), 125.9, 126.8 (2C), 128.3 (2C), 128.4 (2C), 128.5 (2C), 131.3, 134.8, 141.7 (ArC), 134.1 (*CH*=CH_2), 167.0 (C=O); *m*/*z* 279 (M^+, <1%), 238 (20), 122 (20), 117 (13), 105 (100), 91 (11), 77 (31).

4.5.11. (*R*)-*N*-(1-Octylbut-3-enyl)benzamide *ent*-3ge

White solid; mp 68–69 °C; R_f 0.44 (hexane/ethyl acetate: 4/1); $[\alpha]_D^{20} = +11.5$ (*c* 0.5, $CHCl_3$, 72% ee); *v* (film) 3019 (HC=C), 1653 (C=O), 1517 (N–C=O), 1216 cm^{-1} (CN); δ_H 0.87 (t, 3H, *J* = 6.9 Hz, Me), 1.17–1.67 [m, 14H, $(CH_2)_7$], 2.27–2.45 (m, 2H, CH_2CH=CH_2), 4.22 (ddt, 1H, *J* = 14.0, 7.8, 6.3 Hz, CHN), 5.10 (d, 1H, *J* = 10.6 Hz, 1 × *CH*H=C), 5.12 (d, 1H, *J* = 16.6 Hz, 1 × *CH*H=C), 5.84 (ddt, 1H, *J* = 16.6, 10.6, 7.3 Hz, *CH*=CH_2), 7.39–7.77 (m, 5H, ArH); δ_C 14.1 (Me), 22.6, 26.0, 29.2, 29.46, 29.49, 31.8, 34.4 [$(CH_2)_7$], 39.1 (CH_2CH=CH_2), 48.9 (CHN), 117.9 (CH_2=C), 126.7 (2C), 128.5 (2C), 131.2, 135.0 (ArC), 134.4 (*CH*=CH_2), 167.0 (C=O); *m*/*z* 287 (M^+, <2%), 246 (40), 105 (100), 77 (17); HRMS: M^+ found 287.2214, $C_{19}H_{29}NO$ requires 287.2249.

4.5.12. (*R*)-Ethyl 2-benzamido-2-phenylbutanoate 7a[11b]

Yellow oil; R_f 0.50 (hexane/ethyl acetate: 3/1); $[\alpha]_D^{20} = -4.2$ (*c* 0.8, $CHCl_3$, 92% ee); *v* (film) 3412 (NH), 3014 (HC=C), 1723 (C=O), 1667 (C=O), 1512 (N–C=O), 1244 (CO), 1217 cm^{-1} (CN); δ_H 0.93 (t, 3H, *J* = 7.3 Hz, *Me*CH_2C), 1.19 (t, 3H, *J* = 7.1 Hz, *Me*CH_2O), 2.61 (dq, 1H, *J* = 13.9, 7.1 Hz, 1 × *CH*HCN), 3.07 (dq, 1H, *J* = 13.9, 7.3 Hz, 1 × *CH*HCN), 4.13 (dq, 1H, *J* = 10.7, 7.1 Hz, 1 × *CH*HO), 4.26 (dq, 1H, *J* = 10.7, 7.1 Hz, 1 × *CH*HO), 7.24–7.87 (m, 11H, NH and ArH); δ_C 8.6 (*Me*CH_2C), 13.9 (*Me*CH_2O), 25.5 (CH_2C), 62.4 (CH_2O), 66.5 (CN), 125.9 (2C), 127.0 (2C), 127.7, 128.4 (2C), 128.6 (2C), 131.6, 135.3, 139.8 (ArC), 165.3 (CONH), 175.6 (CO_2Et); *m*/*z* 311 (M^+, 1%), 239 (12), 238 (67), 105 (100), 77 (28).

4.5.13. (*R*)-Ethyl 2-benzamido-2,3-diphenylpropanoate 7b

Yellow oil; R_f 0.48 (hexane/ethyl acetate: 3/1); $[\alpha]_D^{20} = +40.1$ (*c* 1, $CHCl_3$, 80% ee); *v* (film) 3411 (NH), 3013 (HC=C), 1728 (C=O), 1666 (C=O), 1510 (N–C=O), 1255 (CN), 1215 cm^{-1} (CO); δ_H 1.22 (t, 3H, *J* = 7.1 Hz, Me), 3.94, 4.29 (2d, 1H each, *J* = 13.1 Hz each, CH_2Ph), 4.19, 4.20 (2qd, 1H each, *J* = 7.1, 3.7 Hz each, CH_2O), 7.09–7.71 (m, 15H, ArH); δ_C 13.8 (Me), 38.0 (CH_2Ph), 62.5 (CH_2O), 66.7 (CN), 125.9 (2C), 126.9 (2C), 127.0, 127.8, 128.2 (2C), 128.50 (2C), 128.53 (2C), 130.0 (2C), 131.5, 134.9, 136.2, 139.7 (ArC), 166.0 (CONH), 172.4 (CO_2Et); *m*/*z* 373 (M^+, <1%), 282 (42), 252 (24), 105 (100), 77 (25); HRMS: $M^+-C_7H_7$, found 282.1108, $C_{17}H_{16}NO_3$ requires 282.1130.

4.5.14. (*R*)-Ethyl 2-benzamido-3-methyl-2-phenylbutanoate 7c

Yellow oil; R_f 0.43 (hexane/ethyl acetate: 3/1); $[\alpha]_D^{20} = -5.2$ (*c* 1, $CHCl_3$, 62% ee); *v* (film) 3404 (NH), 3018 (HC=C), 1724 (C=O), 1671 (C=O), 1511 (N–C=O), 1287 (CO), 1216 cm^{-1} (CN); δ_H 1.03, 1.05 (2d, 3H each, *J* = 6.9 Hz each, Me_2CH), 1.20 (t, 3H, *J* = 7.1 Hz, $MeCH_2$), 3.27 (septet, 1H, *J* = 6.7 Hz, *CH*Me_2), 4.15–4.29 (m, 2H, CH_2O), 7.25–7.85 (m, 10H, ArH); δ_C 14.0 (*Me*CH_2), 18.48, 18.50 (Me_2CH), 33.1 (CHMe), 62.1 (CH_2), 69.5 (CN), 126.9 (2C), 127.1 (2C), 127.4, 128.0 (2C), 128.6 (2C), 131.5, 135.0, 137.6 (ArC), 165.9 (CONH), 172.7 (CO_2Et); *m*/*z* 325 (M^+, <1%), 282 (27), 252 (33), 204 (11), 105 (100), 104 (12), 77 (26); HRMS: $M^+-C_3H_7$, found 282.1145, $C_{17}H_{16}NO_3$ requires 282.1130.

4.6. Oxidation of the benzamides. Isolation of the amino acids 4, *ent*-4 and 8: General procedure

The reductive cleavage of the terminal C=C bond of compounds **3a–e** and *ent*-**3ga–ge** or the furyl group of compounds **3fa–fe** was carried out by treatment with $NaIO_4$ in the presence of a catalytic amount of $RuCl_3$, following a literature procedure.[19] The expected amino acids **4**, *ent*-**4** and **8** were obtained in the yields indicated in Tables 1 and 2. Their corresponding physical, spectroscopic and analytical data follow.

4.6.1. (*S*)-2-Benzamido-2-phenylacetic acid 4a[28]

White solid; mp 199–200 °C; $[\alpha]_D^{20} = +58.0$ (*c* 0.7, $CHCl_3$, 94% ee); *v* (film) 3400 (NH and OH), 3063 (HC=C), 1731 (C=O), 1643 (C=O), 1524 (N–C=O), 1099 cm^{-1} (CN); δ_H 5.78 (br s, 1H, CH), 7.33–7.60, 7.78–7.88 (2m, 9H and 2H, respectively, ArH and NH), 9.60 (s, 1H, CO_2H); δ_C 64.0 (CHN), 127.2 (2C), 127.4, 128.1 (2C), 128.7 (2C), 129.0 (2C), 129.1, 129.5, 132.0 (ArC), 166.9 (CONH), 170.8 (CO_2H); *m*/*z* 210 (M^+-CO_2H, 38%), 193 (10), 105 (100), 77 (37).

4.6.2. (*S*)-2-Benzamido-2-(4-chlorophenyl)acetic acid 4b[40]

White solid; mp 181–182 °C; $[\alpha]_D^{20} = +49.0$ (*c* 1, $CHCl_3$, 92% ee); *v* (film) 3410 (NH and OH), 1728 (C=O), 1645 (C=O), 1522 (N–C=O), 1092 cm^{-1} (CN); δ_H 5.68 (d, 1H, *J* = 6.4 Hz, CHN), 7.24–7.62, 7.66–7.85 (2m, 8H and 2H, respectively, ArH and NH), 9.30 (br s, 1H, CO_2H); δ_C 56.4 (CHN), 127.2 (2C), 128.65 (2C), 128.73 (2C), 128.8, 129.0, 129.1 (2C), 132.2, 134.5 (ArC), 167.3 (CONH), 173.4 (CO_2H); *m*/*z* 245 (M^+-CO_2, 16%), 244 (28), 105, (100), 77 (49), 51 (15).

4.6.3. (*S*)-2-Benzamido-2-(4-methoxyphenyl)acetic acid 4c[41]

Colourless oil; $[\alpha]_D^{20} = +31.0$ (*c* 1, $CHCl_3$, 88% ee); *v* (film) 3417 (NH and OH), 1714 (C=O), 1639 (C=O), 1601 (N–C=O), 1244 (CO), 1108 cm^{-1} (CN); δ_H 3.80 (s, 3H, Me), 5.72 (s, 1H, CHN), 6.88–8.10 (m, 10H, ArH and NH), 9.62 (br s, 1H, CO_2H); δ_C 55.3 (Me), 63.3 (CHN), 114.9 (2C), 127.1 (2C), 128.58 (2C), 128.63, 128.7, 129.5 (2C), 132.0, 160.1, 166.8 (CONH), 170.0 (CO_2H); *m*/*z* 251 (M^+-CO_2, 26%), 240 (78), 105 (100), 103 (59), 77 (65), 76 (26), 51 (25).

4.6.4. (*S*)-2-Benzamido-4-phenylbutanoic acid 4d[42]

Colourless oil; $[\alpha]_D^{20} = +7.2$ (*c* 0.4, $CHCl_3$, 58% ee); *v* (film) 3321 (NH and OH), 3024 (HC=C), 1727 (C=O), 1638 (C=O), 1520 (N–C=O), 1216 cm^{-1} (CN); δ_H 2.15–2.25, 2.32–2.42 (2m, 1H each, CH_2CN), 2.78 (t, 2H, *J* = 8.5 Hz, CH_2Ph), 4.78 (td, 1H, *J* = 7.3, 5.2 Hz, CHN), 6.73 (br s, 1H, NH), 7.18–7.70 (m, 10H, ArH); δ_C 31.7 (CH_2Ph), 33.4 (CH_2CN), 52.7 (CHN), 126.3, 127.1 (2C), 128.4 (2C), 128.60 (2C), 128.64 (2C), 132.0, 133.3, 140.6 (ArC), 167.7 (CONH), 176.1 (CO_2H); *m*/*z* (DIP) 283 (M^+, <1%), 179 (63), 161 (59), 105 (100), 91 (11), 77 (37).

4.6.5. (*S*)-2-Benzamidodecanoic acid 4e[43]

Colourless oil; $[\alpha]_D^{20} = +6.1$ (*c* 0.4, MeOH, 60% ee); *v* (film) 3429 (NH and OH), 3019 (HC=C), 1720 (C=O), 1656 (C=O), 1519 (N–C=O), 1215 cm^{-1} (CN); δ_H 0.87 (t, 3H, *J* = 6.8 Hz, Me), 1.20–1.47 [m, 12H, $(CH_2)_6$Me], 1.77–1.88, 1.97–2.06 (2m, 1H each, CH_2CN), 4.81 (td, 1H, *J* = 7.4, 5.6 Hz, CHN), 6.74 (d, 1H, *J* = 7.4 Hz, NH), 7.45, 7.53, 7.81 (t, t and d, respectively, 2H, 1H and 2H, respectively, *J* = 7.5 Hz each, ArH); δ_C 14.1 (Me), 22.6, 25.3, 29.17, 29.22, 29.3, 31.8, 32.2 [$(CH_2)_7$], 52.8 (CHN), 127.1 (2C), 128.6 (2C), 132.0, 133.6 (ArC), 167.7 (CONH), 176.3 (CO_2H); *m*/*z* (DIP) 291 (M^+, 1%), 246 (10), 179 (26), 161 (17), 105 (100), 77 (20).

4.6.6. (*R*)-2-Benzamidobutanoic acid *ent*-4fa[44]

Brown oil; $[\alpha]_D^{20} = -14.0$ (*c* 0.3, MeOH, 92% ee); *ν* (film) 3309 (NH and OH), 1743 (C=O), 1622 (C=O), 1537 (N–C=O), 1183 cm^{-1} (CN); δ_H (MeOH-d_4) 1.03 (t, 3H, *J* = 7.4 Hz, Me), 1.80 (dq, 1H, *J* = 14.3, 7.1 Hz, 1 × C*H*H), 2.07 (dq, 1H, *J* = 14.3, 6.9 Hz, 1 × C*H*H), 4.48 (q, 1H, *J* = 6.5 Hz, CHN), 7.44, 7.56, 7.86 (t, t and d, respectively, 2H, 1H and 2H, respectively, *J* = 7.3 Hz each, ArH); δ_C (MeOH-d_4) 10.9 (Me), 26.0 (CH_2), 56.4 (CHN), 128.4 (2C), 129.5 (2C), 132.8, 135.4 (ArC), 170.3 (CONH), 176.9 (CO_2H); *m*/*z* 207 (M^+, <1%), 122 (21), 117 (13), 105 (100), 91 (10), 77 (29).

4.6.7. (*R*)-2-Benzamido-4-methylpentanoic acid *ent*-4fb[45]

Dark oil; $[\alpha]_D^{20} = -10.0$ (*c* 0.3, MeOH, 96% ee); *ν* (film) 1739 (C=O), 1627 (C=O), 1564 (N–C=O), 1163 cm^{-1} (CN); δ_H (MeOH-d_4) 0.97, 0.99 (2d, 3H each, *J* = 6.2 Hz each, Me_2CH), 1.69–1.88 (m, 3H, CH_2CN), 4.69 (dd, 1H, *J* = 10.0, 4.6 Hz, CHN), 7.44 (dd, 2H, *J* = 7.4, 7.0 Hz, 2 × ArH), 7.52 (t, 1H, *J* = 7.4 Hz, 1 × ArH), 7.86 (d, 2H, *J* = 7.0 Hz, 2 × ArH); δ_C (MeOH-d_4) 21.8, 23.4 (Me_2CH), 26.2 (CHN), 42.3 (CH_2), 52.6 (CHN), 128.5 (2C), 129.4 (2C), 132.8, 135.3 (ArC), 170.4 (CONH), 176.2 (CO_2H); *m*/*z* 235 (M^+, <1%), 179 (28), 161 (17), 105 (100), 77 (29).

4.6.8. (*R*)-2-Benzamidoheptanoic acid *ent*-4fc[46]

Dark oil; $[\alpha]_D^{20} = -5.0$ (*c* 0.5, MeOH, 92% ee); *ν* (film) 3349 (NH and OH), 1641 (C=O), 1610 (C=O), 1575 (N–C=O), 1419 cm^{-1} (CN); δ_H (MeOH-d_4) 0.87 (t, 3H, *J* = 6.3 Hz, Me), 1.23–1.48 [m, 6H, (CH_2)$_3$Me], 1.73–2.01 (m, 2H, CH_2CN), 4.50 (dd, 1H, *J* = 8.3, 5.0 Hz, CHN), 7.42, 7.51, 7.86 (t, t and d, respectively, 2H, 1H and 2H, respectively, *J* = 7.2 Hz each, ArH); δ_C (MeOH-d_4) 14.4 (Me), 23.6, 26.9, 32.7, 33.1 [(CH_2)$_4$], 56.0 (CHN), 128.5 (2C), 129.5 (2C), 132.7, 135.4 (ArC), 169.9 (CONH), 179.1 (CO_2H); *m*/*z* 231 (10), 174 (15), 161 (11), 147 (41), 106 (10), 105 (100), 104 (12), 77 (35).

4.6.9. (*R*)-2-Benzamido-3-phenylpropanoic acid *ent*-4fd[28]

Colourless oil; $[\alpha]_D^{20} = -17.5$ (*c* 0.5, MeOH, 92% ee); *ν* (film) 3091, 3058, 3016 (HC=C), 1720 (C=O), 1612 (C=O), 1537 (N–C=O), 1227 cm^{-1} (CN); δ_H 3.26, 3.37 (2dd, 1H each, *J* = 13.9, 5.6 Hz each, CH_2), 5.08 (dt, 1H, *J* = 7.3, 5.6 Hz, CHN), 6.70 (d, 1H, *J* = 7.3 Hz, NH), 7.16–7.71 (m, 10H, ArH); δ_C 37.3 (CH_2), 53.6 (CHN), 127.1, 127.2 (2C), 128.6 (4C), 129.4 (2C), 131.9, 133.5, 135.7 (ArC), 167.6 (CONH), 175.0 (CO_2H); *m*/*z* (DIP) 269 (M^+, 2%), 148 (66), 147 (21), 105 (100), 91 (14), 77 (34).

4.6.10. (*R*)-2-Benzamido-3-methylbutanoic acid *ent*-4fe[47]

Yellow oil; R_f 0.48 (hexane/ethyl acetate: 3/1); $[\alpha]_D^{20} = -27.6$ (*c* 0.3, $CHCl_3$, 92% ee); *ν* (film) 3452 (NH and OH), 1709 (C=O), 1642 (C=O), 1535 (N–C=O), 1248 cm^{-1} (CN); δ_H 1.03, 1.05 (2d, 3H each, *J* = 7.1 Hz each, Me_2CH), 2.30–2.41 (m, 1H, C*H*Me_2), 4.78 (dd, 1H, *J* = 8.3, 4.8 Hz, CHN), 7.47, 7.52, 7.80 (t, t and d, respectively, 2H, 1H and 2H, respectively, *J* = 7.2 Hz each, ArH), 8.08 (d, 1H, *J* = 8.3 Hz, NH); δ_C 17.8, 19.1 (Me_2CH), 31.3 (C*H*Me_2), 57.5 (CHN), 127.1 (2C), 128.7 (2C), 131.9, 133.8 (ArC), 167.9 (CONH), 175.9 (CO_2H); *m*/*z* 221 (M^+, <1%), 161 (56), 133 (18), 106 (21), 105 (100), 77 (47), 51 (13).

4.6.11. (*S*)-3-Benzamido-3-phenylpropanoic acid 8a[48]

Yellow solid; mp 189–190 °C; $[\alpha]_D^{20} = +73.0$ (*c* 1.5, $CHCl_3$, 88% ee); *ν* (film) 3347 (NH and OH), 1695 (C=O), 1637 (C=O), 1522 (N–C=O), 1282 cm^{-1} (CN); δ_H (MeOH-d_4) 2.95, 3.00 (2dd, 1H each, *J* = 16.0, 5.9 Hz each, CH_2), 5.61 (t, 1H, *J* = 5.9 Hz, CHN), 7.23–7.84 (m, 10H, ArH); δ_C (MeOH-d_4) 41.5 (CH_2), 52.1 (CHN), 127.6 (2C), 128.36 (2C), 128.42 (2C), 129.5 (2C), 129.6, 132.7, 135.7, 143.1 (ArC), 169.0 (CONH), 173.5 (CO_2H); *m*/*z* (DIP) 269 (M^+, <1%), 164 (88), 105 (100), 104 (17), 77 (42).

4.6.12. (*S*)-3-Benzamido-3-(4-chlorophenyl)propanoic acid 8b[49]

White solid; mp 190–191 °C; $[\alpha]_D^{20} = +4.0$ (*c* 0.5, MeOH, 92% ee); *ν* (film) 3328 (NH and OH), 1701 (C=O), 1638 (C=O), 1524 cm^{-1} (N–C=O); δ_H 2.91, 2.97 (2dd, 1H each, *J* = 15.9, 6.4 Hz each, CH_2), 4.34 (br s, 2H, NH and CO_2H), 5.56 (t, 1H, *J* = 6.4 Hz, CHN), 7.30, 7.36 (2d, 2H each, *J* = 8.6 Hz each, 4 × ArH), 7.41–7.84 (m, 5H, 5 × ArH); δ_C 39.4 (CH_2), 49.4 (CHN), 126.8 (2C), 127.5 (2C), 128.2 (2C), 128.4 (2C), 131.5, 132.9, 133.6, 139.4 (ArC), 167.4 (CONH), 173.1 (CO_2H); *m*/*z* (DIP) 305 (M^++2, <1%), 303 (M^+, 2%), 200 (26), 198 (80), 138 (12), 105 (100), 77 (36).

4.6.13. (*R*)-3-Benzamido-5-phenylpentanoic acid 8d

Yellowish solid; mp 139–140 °C; $[\alpha]_D^{20} = +10.8$ (*c* 1, $CHCl_3$, 70% ee); *ν* (film) 3301 (NH and OH), 1694 (C=O), 1638 (C=O), 1533 (N–C=O), 1250 cm^{-1} (CN); δ_H 1.95 (dtd, 1H, *J* = 14.2, 8.3, 5.6 Hz, 1 × CH_2C*H*HCN), 2.07 (dq, 1H, *J* = 14.2, 8.3 Hz, 1 × CH_2C*H*HCN), 2.63 (dd, 1H, *J* = 15.8, 5.2 Hz, 1 × C*H*HCO_2H), 2.68 (dd, 1H, *J* = 15.8, 5.2 Hz, 1 × C*H*HCO_2H), 2.72 (t, 2H, *J* = 8.0 Hz, CH_2Ph), 4.04 (br s, 2H, NH and CO_2H), 4.48 (dq, 1H, *J* = 8.8, 5.3 Hz, CHN), 7.13–7.77 (m, 10H, ArH); δ_C 32.5 (CH_2Ph), 35.6 (CH_2CH_2Ph), 38.2 (CH_2CO_2H), 46.3 (CHN), 125.8, 126.8 (2C), 128.2 (2C), 128.3 (2C), 128.4 (2C), 131.5, 134.1, 141.2 (ArC), 167.5 (CONH), 174.1 (CO_2H); *m*/*z* (DIP) 297 (M^+, 8%), 193 (36), 105 (100), 88 (37), 77 (38).

4.6.14. (*R*)-3-Benzamidoundecanoic acid 8e[50]

Yellow solid; mp 130–131 °C; $[\alpha]_D^{20} = +7.5$ (*c* 0.5, MeOH, 72% ee); *ν* (film) 3299 (NH and OH), 1699 (C=O), 1639 (C=O), 1537 (N–C=O), 1317 cm^{-1} (CN); δ_H 0.86 (t, 3H, *J* = 6.7 Hz, Me), 1.19–1.40 [m, 12H, (CH_2)$_6$Me], 1.57–1.74 (m, 2H, CH_2CH_2CN), 2.66 (dd, 1H, *J* = 16.2, 5.0 Hz, 1 × C*H*HCO_2H), 2.73 (dd, 1H, *J* = 16.2, 4.9 Hz, 1 × C*H*HCO_2H), 4.38–4.51 (m, 1H, CHN), 6.90 (d, 1H, *J* = 9.0 Hz, NH), 7.38–7.79 (m, 5H, ArH); δ_C 14.1 (Me), 22.6, 26.3, 29.2, 29.3, 29.4, 31.8, 34.1 [(CH_2)$_7$], 38.3 (CH_2CO_2H), 46.4 (CHN), 126.9 (2C), 128.6 (2C), 131.6, 134.2 (ArC), 167.3 (CONH), 176.4 (CO_2H); *m*/*z* 305 (M^+, 4%), 200 (12), 193 (13), 192 (17), 122 (18), 105 (100), 77 (23).

4.6.15. (*S*)-*N*-[1-(4-Methoxyphenyl)-2-formylethyl]benzamide 9[51]

Orange oil; R_f 0.50 (hexane/ethyl acetate: 3/1) $[\alpha]_D^{20} = +15.0$ (*c* 1, $CHCl_3$, 92% ee); *ν* (film) 3349 (NH), 1720 (C=O), 1662 (C=O), 1513 (N–C=O), 1098 cm^{-1} (CN); δ_H 3.00 (ddd, 1H, *J* = 16.8, 6.2, 1.2 Hz, 1 × C*H*H), 3.17 (ddd, 1H, *J* = 16.8, 6.6, 2.3 Hz, 1 × C*H*H), 3.78 (s, 3H, Me), 5.65 (dt, 1H, *J* = 7.6, 6.5 Hz, CHN), 7.00 (d, 1H, *J* = 7.6 Hz, NH), 6.83–7.76 (m, 9H, ArH), 9.78 (dd, 1H, *J* = 2.3, 1.2 Hz, CHO); δ_C 48.6 (CHN), 48.8 (CH_2), 55.2 (Me), 114.2 (2C), 127.0 (2C), 127.7 (2C), 128.6 (2C), 131.7, 132.3, 133.9, 159.1 (ArC), 166.7 (CONH), 200.7 (CHO); *m*/*z* (DIP) 283 (M^+, 1%), 240 (20), 149 (13), 135 (42), 134 (11), 105 (100), 85 (14), 83 (10), 77 (52), 72 (21), 71 (23), 69 (12), 58 (51), 57 (22), 55 (15), 43 (35), 41 (12).

4.7. Determination of the enantiomeric excesses of amino acids 4, *ent*-4 and 8

K_2CO_3 (0.7 mmol) and MeI (0.7 mmol) were added to a solution of the amino acid **4**, *ent*-**4** and **8** (0.4 mmol) in anhydrous DMF (4.5 mL) at 0 °C. After stirring overnight at room temperature, water (10 mL) was added and the mixture was extracted with Et_2O (2 × 10 mL). The combined organic layers were dried (Na_2SO_4). After filtration and evaporation of the solvents, the obtained amino esters were analyzed by HPLC on a ChiralCel OD-H column using a 254 nm UV detector, 10% *i*-PrOH in hexane as eluent and a flow rate of 0.5 mL/min. The retention times were 29.9 (**4a** methyl ester; 5% *i*-PrOH in hexane as eluent), 45.4 (*ent*-**4a**

methyl ester; 5% *i*-PrOH in hexane as eluent), 29.7 (*ent*-**4b** methyl ester), 37.1 (**4b** methyl ester), 35.6 (**4c** methyl ester), 42.1 (*ent*-**4c** methyl ester), 37.0 (*ent*-**4d** methyl ester), 44.9 (**4d** methyl ester), 20.5 (*ent*-**4e** methyl ester), 22.1 (**4e** methyl ester), 9.4 (*ent*-**4fa** methyl ester), 12.3 (**4fa** methyl ester), 8.2 (*ent*-**4fb** methyl ester; flow rate 1.0 mL/min), 14.4 (**4fb** methyl ester; flow rate 1.0 mL/min), 6.7 (*ent*-**4fc** methyl ester; flow rate 1.0 mL/min), 9.1 (**4fc** methyl ester; flow rate 1.0 mL/min), 11.6 (*ent*-**4fd** methyl ester; flow rate 1.0 mL/min), 16.6 (**4fd** methyl ester; flow rate 1.0 mL/min), 6.9 (*ent*-**4fe** methyl ester; 2% *i*-PrOH in hexane as eluent, flow rate 2.0 mL/min), 10.3 (**4fe** methyl ester; 2% *i*-PrOH in hexane as eluent, flow rate 2.0 mL/min), 34.1 (*ent*-**8a** methyl ester), 48.2 (**8a** methyl ester), 33.9 (*ent*-**8b** methyl ester), 46.2 (**8b** methyl ester), 23.9 (**8d** methyl ester), 36.7 (*ent*-**8d** methyl ester), 32.7 (*ent*-**8e** methyl ester; 1% *i*-PrOH in hexane as eluent, flow rate 1.0 mL/min), 47.7 (**8e** methyl ester; 1% *i*-PrOH in hexane as eluent, flow rate 1.0 mL/min), 23.5 (**9**), 30.3 (*ent*-**9**). The enantiomeric excesses obtained are collected in Tables 1 and 2.

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