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Diastereoselective synthesis of 2-vinylpyrrolidines and 2-vinylpiperidines by the palladium-catalysed cyclization of amino-allylic carbonates containing a chiral protecting group

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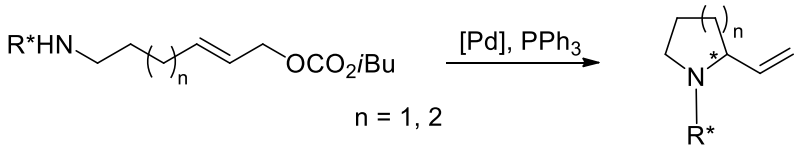
Abstract

An efficient diastereoselective synthesis of pyrrolidine- and piperidine-type N-heterocycles is reported, by the intramolecular Pd(0)-catalysed cyclization of amino carbonates containing chiral protecting group. The use of chiral auxiliary in the cyclization gave the corresponding heterocyclic derivatives in excellent yields and with good dr values.



R* = (*S*)- and (*R*)-$CH(CH_3)C_6H_5$, (*S*)-$CH(CH_2C_6H_5)CO_2CH_3$, (*S*)-$CH(CH_3)CO_2CH_3$, (*S*)-$CH(CH_2CH(CH_3)_2)CO_2CH_3$, (*S*)-$CH(CH(CH_3)_2)CO_2CH_3$

Keywords: Allylic carbonates, cyclization, homogeneous catalysis, nitrogen heterocycles, palladium

Introduction

Saturated nitrogen heterocycles, such as pyrrolidines and piperidines, often possess potent biological activity and are therefore of interest for organic and medicinal chemists.[1-4] For example, piperidine alkaloids are known pharmaceuticals; (-)-prospinine[5] is used as an anesthetic and analgesic, (-)-spectaline[6] has cytotoxic activity and (-)-cassine[7] has antifungal activity. There are many drugs, especially with piperidine rings, for example the well-known Donepezil which has been shown to be well tolerated to improve cognition and global function in patients with mild to moderately severe Alzheimer's disease.[8-9]

On the other hand, these heterocyclic derivatives play an important role in organic synthesis as excellent building blocks for further synthesis. N-Substituted cyclic derivatives containing a vinyl moiety are useful starting materials for olefin cross-metathesis reactions[10] and also excellent intermediates to afford medium and large-ring cyclic structures by 3-aza-Cope rearrangements.[11]

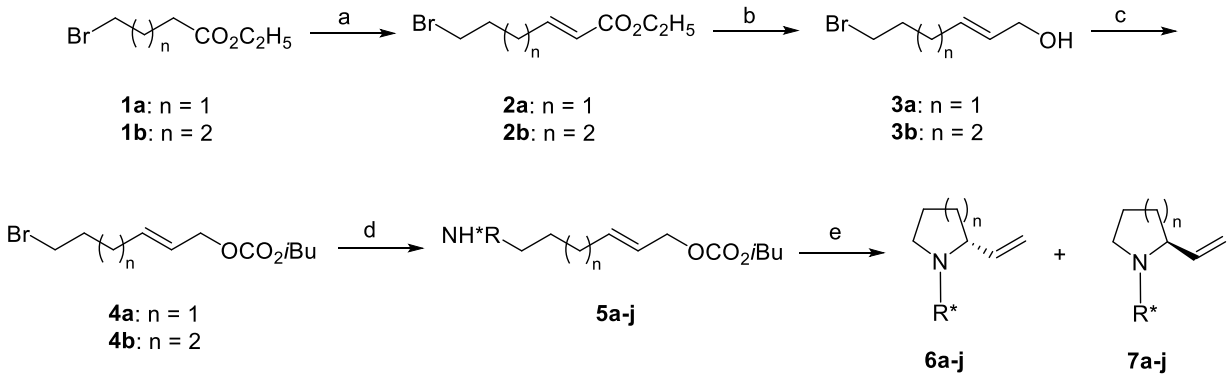
For these reasons, the efficient synthesis of optically active pyrrolidine and piperidine derivatives has been of long-standing interest. Several powerful new transformations have been developed that involve the use of Pd-catalysed C-N bond-forming reactions for construction of heterocyclic rings. This type of transformation frequently occurs under mild conditions, tolerates a broad array of functional groups, and proceeds with high stereoselectivity.[12-34]

Extending our previous work on the use of allylic carbonates in the synthesis of O- and N-heterocycles,[35-40] in this paper we report new results on diastereoselective intramolecular Pd(0)-catalysed allylic aminations. Herein, we present the first examples of asymmetric palladium catalysis in which the starting amino carbonates contain a chiral protecting group with known and specified absolute configuration which can act as a chiral auxiliary and also enable one to perform the cyclization reaction in a stereoselective way, without the presence of any chiral ligands.

Results and Discussion

Synthesis of the starting materials

The starting allylic carbonates **5a-j** (Scheme 1) were prepared by reduction of bromoesters **1a,b** to the corresponding aldehydes,[41] followed by elongation of the chain *via* the Wittig rection,[42] reduction to the alcohol **3a,b**,[43] condensation with isobutyl chloroformate as described previously[37, 40] and finally, the reaction of received bromo-derivatives **4a,b** with the appropriate amines ((*S*)-1-phenylethanamine and (*R*)-1-phenylethanamine) or amino acid ester hydrochlorides, obtained by the procedure described in the literature (derivatives of L-phenylalanine, L-alanine, L-leucine and L-valine).[44-47] This procedure allows us to prepare carbonates (**5a-j**) containing chiral amino protecting group in good yields (21-66%).



a: n = 2, R* = (*S*)-CH(CH$_3$)C$_6$H$_5$
b: n = 2, R* = (*R*)-CH(CH$_3$)C$_6$H$_5$
c: n = 2, R* = (*S*)-CH(CH$_2$C$_6$H$_5$)CO$_2$CH$_3$
d: n = 1, R* = (*S*)-CH(CH$_2$C$_6$H$_5$)CO$_2$CH$_3$
e: n = 1, R* = (*S*)-CH(CH$_3$)CO$_2$CH$_3$
f: n = 2, R* = (*S*)-CH(CH$_3$)CO$_2$CH$_3$
g: n = 1, R* = (*S*)-CH(CH$_2$CH(CH$_3$)$_2$)CO$_2$CH$_3$
h: n = 2, R* = (*S*)-CH(CH$_2$CH(CH$_3$)$_2$)CO$_2$CH$_3$
i: n = 1, R* = (*S*)-CH(CH(CH$_3$)$_2$)CO$_2$CH$_3$
j: n = 2, R* = (*S*)-CH(CH(CH$_3$)$_2$)CO$_2$CH$_3$

reagents and conditions: (a) 1. DIBAL-H, CH_2Cl_2, -78 °C, 2. $Ph_3P{=}CHCO_2C_2H_5$, CH_2Cl_2, rt; (b) DIBAL-H, Et_2O, 0 °C; (c) $(CH_3)_2CHCH_2OCOCl$, C_5H_5N, CH_2Cl_2, 0 °C→rt; (d) RNH_2, *i*-Pr_2EtN, DMF, rt for **5a,b** and RNH_2·HCl, K_2CO_3, CH_3CN, 40 °C for **5c-j**; (e) [Pd], ligand, solvent.

Scheme 1. Pd^0-Catalysed synthesis of heterocycles **6a**-**j**.

Pd$^{0/II}$-Catalysed cyclisation of the allylic carbonates 5a,b

The cyclization was first studied with isobutyl carbonate **5a** as the substrate (Scheme 1) in THF at 0 °C in the presence of a catalytic amount of $Pd_2(dba)_3$ and PPh_3. The course of the reaction was monitored by TLC analysis. After 24 hours in the reaction mixture only the starting compound was observed. The cyclization of carbonate **5b** under these conditions also did not take place (Table 1, Entries 1-2). When the cyclization of **5a** was performed at room temperature, piperidine **7a** was obtained as the single stereoisomer in 94% yield (Table 1, Entry 3), whereas the starting amino carbonate **5b** containing a chiral protecting group with an opposite absolute configuration, gave the cyclization product **6b** containing a reverse configuration at the newly created stereogenic center (Table 1, Entry 4).

Table 1. Pd^0-catalysed allylic cyclization of substrates **5a-b** according to Scheme 1[a]

Entry	Carbonate	[Pd]	Ligand	T [°C]	Yield (**6** + **7**) [%][b]	dr[c] (**6**:**7**)
1	**5a**	Pd_2dba_3	PPh_3	0	traces	-
2	**5b**	Pd_2dba_3	PPh_3	0	traces	-
3	**5a**	Pd_2dba_3	PPh_3	20	94	0:100
4	**5b**	Pd_2dba_3	PPh_3	20	95	100:0
5	**5a**	Pd_2dba_3	PPh_3	60	0[d]	-
6	**5b**	Pd_2dba_3	PPh_3	60	0[d]	-
7	**5a**	Pd_2dba_3	dppb	20	99	0:100
8	**5b**	Pd_2dba_3	dppb	20	99	100:0
9	**5a**	$[PdCl(C_3H_5)]_2$	PPh_3	20	0	-
10	**5b**	$[PdCl(C_3H_5)]_2$	PPh_3	20	0	-

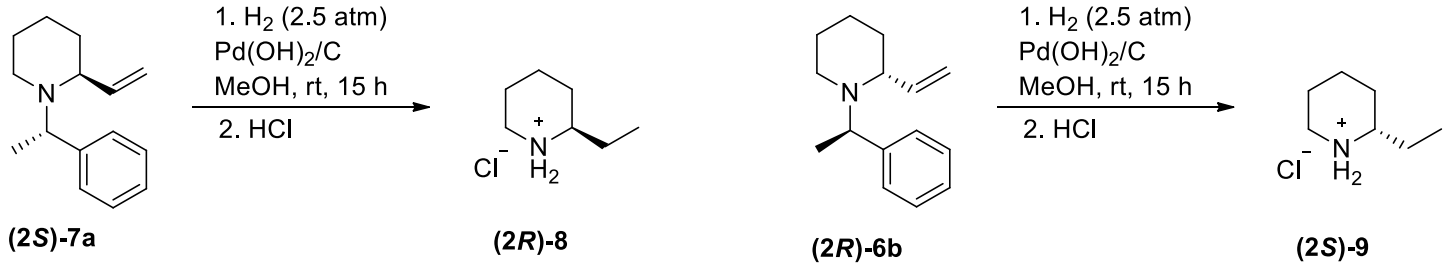
[a] Reaction conditions: [Pd]:[dppb]:[**5**] = 1:2.2:20 or [Pd]:[PPh_3]:[**5**] = 1:4.4:20; THF; 24 hours.
[b] Isolated product. [c] Determined by ^{1}H NMR analysis. [d] Decomposition products.

The same reactions at 60 °C afforded only difficult to identify decomposition products (Table 1, Entries 5-6). When the cyclization reaction of carbonates **5a** and **5b** was performed in the presence of dppb, piperidines **7a** and **6b** were obtained as a single stereoisomer in excellent yields – 99% (table 1, Entries 7-8). We also investigated the effect of the palladium precursor on this reaction but the cyclization products were not observed with the use of the allylpalladium chloride dimer and PPh_3 (Table 1, Entries 9-10).

To determine the relative configuration of the obtained stereoisomers, the cyclisation products **7a** and **6b** were hydrogenolysed in the presence of Pearlman's catalyst $Pd(OH)_2/C$, to give 2-ethylpiperidine in a quantitative yield. In order easily to handle these compounds of high volatility, the crude reaction mixture was treated with a saturated solution of HCl to afford hydrochloride salts **8** and **9** (Scheme 2).

The ^{1}H NMR spectroscopic data and optical rotation for **8** were in excellent agreement with those reported previously for (-)-(2*R*)-2-ethylpiperidine hydrochloride {$[\alpha]_D^{20}$ -1.38 (*c* 0.5, MeOH); lit.[48] $[\alpha]_D^{20}$ -1.42 (*c* 1.8, MeOH), lit.[49] $[\alpha]_D^{20}$ -1.2 (*c* 0.2, EtOH)}. In turn, the optical rotation for **9** was + 1.29 (c 0.5, MeOH), which unambiguously indicates on the (+)-(2S)-2-ethylpiperidine hydrochloride, and hence (*R*)-absolute configuration in the piperidine ring of **6b**.

The received results indicate that the cyclization products **7a** and **6b** have opposite configuration in the piperidine ring, and the stereogenic center located on the N-protecting group of carbonates **5a** and **5b** has a decisive influence on the stereochemical result of the cyclization reaction.



(2*S*)-7a **(2*R*)-8** **(2*R*)-6b** **(2*S*)-9**

Scheme 2. Hydrogenolysis reaction of **7a** and **7b**.

To explain the observed results, we would propose as follows: (i) a six-membered transition state type "chair" for the cyclization reaction, and that the substituents on the nitrogen atom and on the C(2) carbon atom are located in *pseudo*-axial or *pseudo*-equatorial positions in a transition state, (ii) a large volume of the substituent on the nitrogen atom enforces their equatorial orientation (Figure1, **Ia** and **IIa**).

For the equatorial position of the N-nitrogen substituent there are two possible orientations of the vinyl substituent at the C(2) carbon atom (Figure 1, **Ia** and **IIa**). However, there is a strong repulsion between the vinyl moiety in axial position at C(2), and equatorial nitrogen substituent (Figure 1, **IIa**), and therefore the equatorially location of vinyl group (Figure 1, **Ia**) is strongly favored resulting in the formation of *S* product exclusively. The mirror image of **Ia** must be favored for **5b** with (*R*)-configuration (Figure 1, **IIIa**). The products **7a** and **6b** are therefore enantiomers to each other, which is confirmed by opposite values of optical rotation and the identical ^{1}H and ^{13}C NMR spectra recorded for these piperidine derivatives.

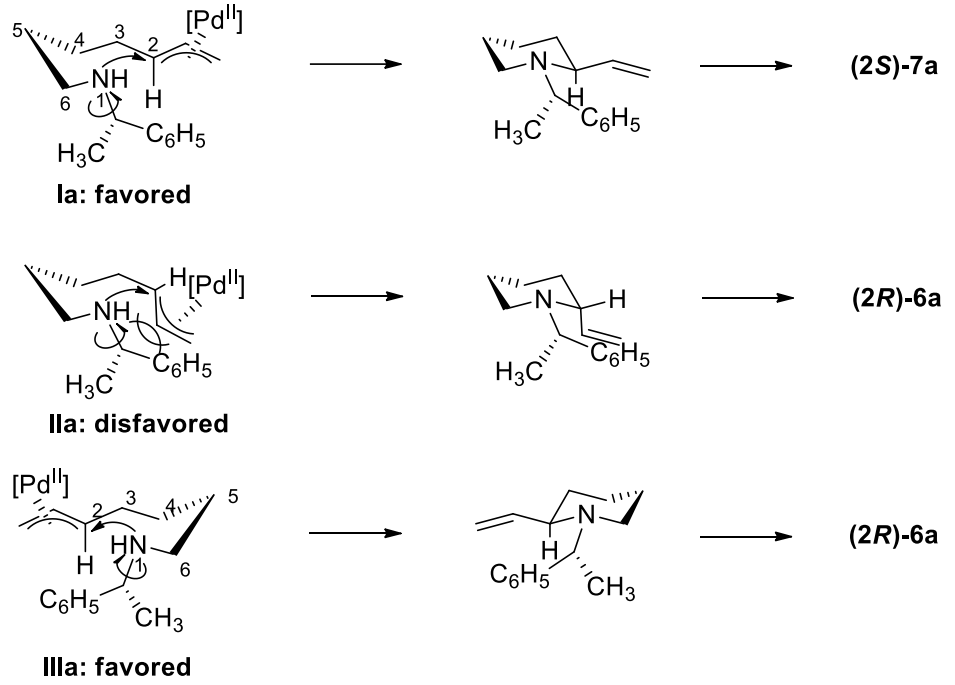


Figure 1. Models for Pd^0-catalysed cyclization of **5a-b.**

In the case of the axial orientation of the nitrogen substituent, there is a strong 1,3-diaxal repulsion with a hydrogen atom at C(5) regardless of the orientation (axial or equatorial) of the remaining substituents (Figure 2, **IVa** and **Va**). These interactions allows to exclude transition states with axial orientation of substituents on the nitrogen atom.

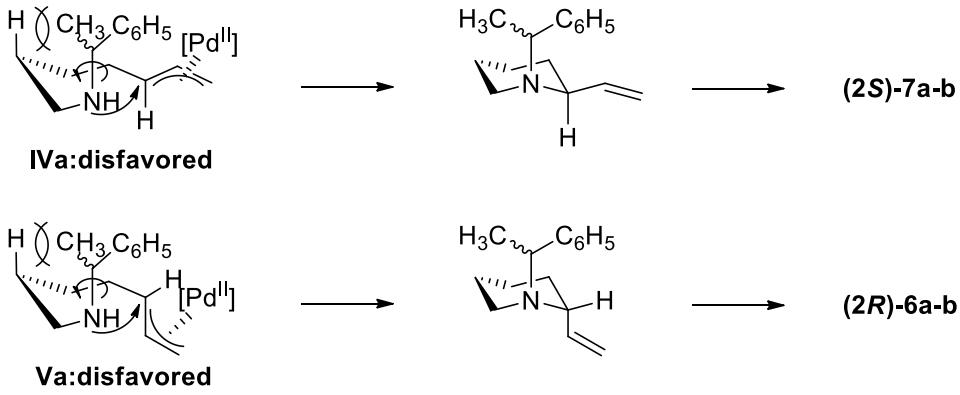


Figure 2. Models for Pd^0-catalysed cyclization of **5a-b**.

Taking in to account above, we can concluded that, the orientation of the substituents on the C(2) carbon atom determines the product configuration and the equatorial location of the N-protecting group allows the aforementioned cyclisation.

Pd^0-Catalysed cyclization of the allylic carbonates 5c-j

Encouraged by the positive results for the carbonates **5a** and **5b** we decided to carry out the cyclization of the other carbonates containing chiral amino protecting group (**5c-j**). As the first, we chose a L-phenylalanine

derivative **5c** (Table 2). The reaction performed in tetrahydrofuran at room temperature in the presence of a catalytic amount of Pd_2dba_3/dppb gave a separable mixture of piperidines **6c** and **7c** in a 45:55 ratio and in 99% overall yield (Table 2, Entry 1). Reaction with dppe as the ligand afforded **6c** and **7c** in a good yield of 98% and with a diastereomeric ratio of 34:66 (Table 2, Entry 2). When PPh_3 was used, a mixture of piperidines **6c** and **7c** was obtained in a 34:66 ratio with 99% overall yield (Table 1, Entry 3). Decreasing the temperature to 0 °C allowed to obtain the final products **6c** and **7c** in lower yield (60%) after 24 h but with significantly higher diastereoselectivity 23:77 (Table 2, Entry 4). On the other hand, increasing temperature to 60 °C gave a mixture of diastereoisomers in a 34:66 ratio (Table 2, Entry 5).

We also investigated the effect of the solvent on this cyclization reaction (Table 2, Entries 6-7). In CH_2Cl_2, products **6c** and **7c** was obtained as a 36:64 mixture of diastereoisomers in 99% overall yield. The use of CH_3CN provided good yield: 98% and a low dr value of 45:55.

Table 2. Effect of the phosphine and solvent on the allylic amination of substrate **5c**[a]

Entry	Ligand	Solvent	T [°C]	Yield (**6** + **7**) [%][b]	dr[c] (**6**:*7*)
1	dppb	THF	20	99	45:55
2	dppe	THF	20	98	34:66
3	PPh_3	THF	20	99	34:66
4	PPh_3	THF	0	60	23:77
5	PPh_3	THF	60	98	34:66
6	PPh_3	CH_2Cl_2	20	99	36:64
7	PPh_3	CH_3CN	20	98	45:55

[a] Reaction conditions: [Pd_2dba_3]:[dppb/dppe]:[**5c**] = 1:2.2:20 or [Pd_2dba_3]:[PPh_3]:[**5c**] = 1:4.4:20; 24 hours.

[b] Isolated product. [c] Determined by ^{1}H NMR analysis.

The structures of the diastereomeric piperidines **6c** and **7c** were confirmed by IR, ^{1}H-NMR, ^{13}C-NMR, ^{1}H-^{1}H COSY and ^{1}H-^{13}C HMQC spectra. The most characteristic difference was observed for the vinyl substituent located on the 2-position of the piperidine ring. The diastereoisomer designated as **6c**, characterized by a lower polarity (R_f = 0.83 hexane/ethyl acetate, 3: 1) gave the signals from the protons of the vinyl moiety at lower values of ppm: 5.03 (dd, CH=CH_2), 5.15 (dd, CH=CH_2) and 5.39 (ddd, CH=CH_2). Diastereomer **7c** (the more polar, R_f = 0.70 hexane/ethyl acetate, 3: 1) gave signals respectively at 5.18 (dd, CH=CH_2), 5.28 (dd, CH=CH_2) and 5.89 (ddd, CH=CH_2).

The configuration of the isomeric products **6c** and **7c** was assigned based on the results obtained for (*S*)-1-((*S*)-1-phenylethyl)-2-vinylpiperidine **7a** and (*R*)-1-((*R*)-1-phenylethyl)-2-vinylpiperidine **6b**. We believe that the sense of asymmetric induction was the same and the major product of cyclization **5c** corresponded to diastereomer **7c** with an absolute *S* configuration on the 2-position of the piperidine ring. It should be noted that higher values of chemical shifts of the vinylic protons of diastereoisomer (2*S*)-**7c** than (2*R*)-**6c** are in accord with literature data described by Fox and Gallagher for *N*-substituted-2-vinylpyrrolidine derivatives.[50]

Taking into account the results obtained for **5c**, the cyclizations of amino carbonates **5d-j** were performed in THF and CH_2Cl_2 in the presence of PPh_3 as a ligand. Although the cyclization reaction with dppe as a ligand gave similar results, we decided to use PPh_3 for further study for economic reasons.

The ring-closure of **5d** occurred easily at room temperature in THF and provided 2-vinylpyrrolidines (2*R*)-**6d** and (2*S*)-**7d** as a 27:73 separable mixture of diastereoisomers in 99% yield (Table 3, Entry 1). The same

reaction in methylene chloride afforded a 33:67 mixture of diasteroisomers (Table 3, Entry 2). In these tests, the major isomer again corresponded to the more polar isomer **7d** ($R_{f\mathbf{6d}}$ = 0.81; $R_{f\mathbf{7d}}$ = 0.65; hexane/ethyl acetate 3:1) and gave the signals of the vinylic protons at lower values of field (4.99, 5.12, 5.35 ppm for (2*R*)-**6d** and 5.15, 5.24, 5.86 ppm for **7d**). The absolute configuration of **6d** and **7d** was assigned based on the results obtained with piperidine derivatives **6a-c** and **7a-c** and the literature data for *N*-substituted-2-vinylpyrrolidine derivatives.[50]

Table 3 Pd^0-Catalysed allylic amination of substrates **5d-j**[a]

Entry	Carbonate	Solvent	T [°C]	Conv. (**6** + **7**) [%][b]	dr[b] (**6**:**7**)
1	**5d**	THF	20	99[c]	27:73
2	**5d**	CH_2Cl_2	20	99[c]	33:67
3	**5e**	THF	20	0	-
4	**5e**	THF	60	100	45:55
5	**5e**	CH_2Cl_2	35	100	48:52
6	**5f**	THF	20	100	42:58
7	**5f**	CH_2Cl_2	20	100	42:58
8	**5g**	THF	20	100	27:73
9	**5g**	CH_2Cl_2	20	100	34:66
10	**5h**	THF	20	0	-
11	**5h**	THF	60	100	40:60
12	**5h**	CH_2Cl_2	35	100	38:62
13	**5i**	THF	20	100	27:73
14	**5j**	THF	20	45	30:70
15	**5j**	THF	60	45	30:70

[a] Reaction conditions: $[Pd_2dba_3]$:$[PPh_3]$:[**5**] = 1:4.4:20; THF; 24 hours.

[b] Determined by ^{1}H NMR analysis.

[c] Isolated product.

The cyclization of alanine derivative **5e** in THF at room temperature did not give the expected products **6e** and **7e** (Table 3, Entry 3). The reaction at 60 °C afforded pyrrolidines **6e** and **7e** in 100% conversion with a dr of 45:55 after 20 h (Table 3, Entry 4). The reaction carried out in methylene chloride gave **6e** and **7e** with a very good yield but lower diastereoselectivity: dr = 48:52 (Table 3, Entry 5).

Amino carbonate **5f** with a longer chain already at room temperature in THF gave the diastereomeric piperidines **6f** and **7f** in 100% conversion and dr = 42:58 Similar results were obtained for the reaction carried out in methylene chloride (Table 3, Entries 6-7). Unfortunately, an attempt to separate the resulting products was not successful but their structures were determined using spectroscopic methods. Cyclization of L-leucine derivative **5g** at room temperature in THF gave an 27:73 inseparable mixture of stereoisomeric pyrrolidines **6g** and **7g** in 100% conversion (Table 3, Entry 8). Significantly lower level of diastereoselectivity was observed when the reaction was performed with the same amino carbonate **5g** in methylene chloride - 34:66 dr (Table 3, Entry 9). In turn, the longer chain of the leucine derivative **5h** did not undergo the cyclisation in THF at room temperature and in the NMR spectrum of the mixture of reactants no trace of the product was observed, even after prolonging the reaction time to 48 hours (Table 3, Entry 10). Diastereomeric piperidines **6h** and **7h** were obtained in 100% conversion and with a dr ratio of 40:60 after increase the temperature to 60 °C (Table 3,

Entry 11). The reaction performed in methylene chloride at an elevated temperature (35 °C) afforded the desired products in 100% conversion and low dr value of 38:62 (Table 3, Entry 12). Finally, we tested the L-valine derivatives **5i** and **5j** (Table 3, Entries 13-15). Ring-closure of **5i** occurred readily in THF at room temperature and provided quantitatively 2-vinylpyrrolidines **6i** and **7i** as a 27:73 inseparable mixture of diastereoisomers. Carbonate **5j** under these conditions appeared to be less reactive and gave piperidines **6j** and **7j** with a lower yield (45% conversion) and selectivity (30:70 dr). Increasing the temperature to 60 °C did not result in decrease of reaction selectivity and yield. We have not performed the cyclization reactions of carbonates **5i** and **5j** in methylene chloride because the results obtained in earlier tests demonstrated a lower diastereoselectivity the reactions conducted in this solvent.

The stereoselectivities observed in the formation of piperidines **6** and **7** in the Pd-catalyzed cyclization of amino allylic carbonates **5c**,**f**,**h**,**j** could be explained on the base the Figure 3.

We continue to maintain that the substituent on the nitrogen atom should be located in the *pseudo*-equatorial orientation as mentioned previously. Additionally, a *pseudo*-axial orientation of the vinyl substituent on the C(2) carbon atom is necessary for the formation of the (2*R*)-**6** isomer (Figure 3, **IIb**). The size of the substituent plays decisive role in the formation such conformation and therefore the yields of the (2*R*)-**6** stereoisomer for substrates containing a small substituent, e.g. methyl, are higher [dr values (2*R*)-**6f**:(2*S*)-**7f** = 42:58] than for those containing more crowded substituents as benzyl or isopropyl (dr ratio above 33:67). In turn, the formation of a (2*S*)-**7** stereoisomer (Figure 3, **Ib**) can be explained as before for phenylethanamine derivatives (Figure 1, **Ia**).

Similar considerations can be performed for 2-vinylpyrrolidines derivatives (Figure 3, **Ic** and **IIc**). The conformation **Ic** leads to the stereoisomer (2*S*)-**7**, whereas conformation **IIc** leads to the stereoisomer (2*R*)-**6**.

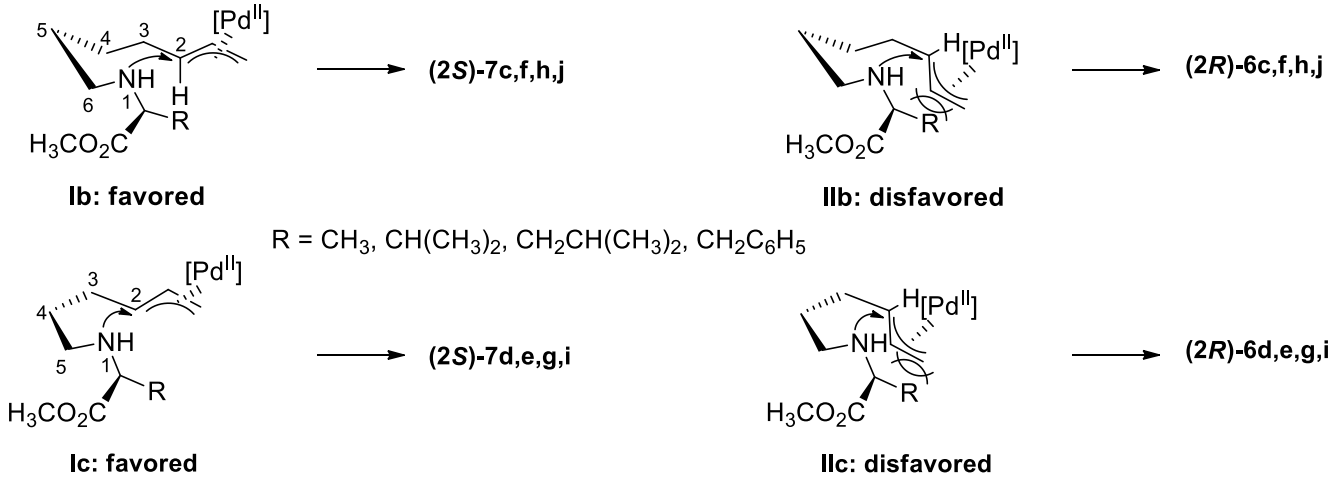
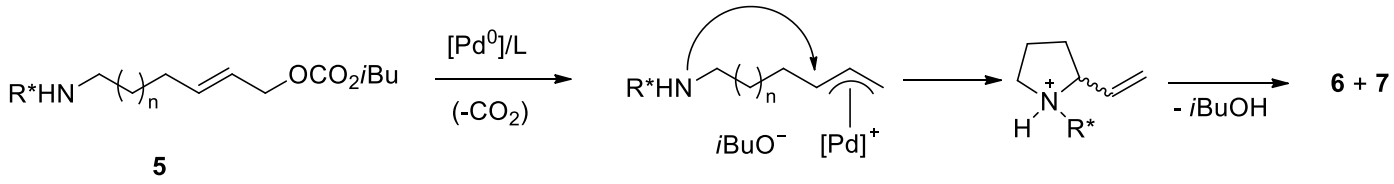


Figure 3. Models for Pd^0-catalysed cyclization of **5c-j.**

The reaction mechanism for this Pd(0)-catalysed cyclization of amino carbonates containing chiral protecting group is shown in Scheme 3. Carbonate **5** reacted with Pd^0 to give η^3-allylPd complex. Attack of the nitrogen nucleophile on the η^3-allyl intermediate followed by deprotonation gave the cyclic compounds **6** and **7**.



Scheme 3. Mechanism of the Pd^0-catalysed cyclization.

Conclusions

In conclusion, we have developed a simple and efficient methodology for the synthesis of chiral nitrogen-containing heterocycles *via* Pd(0)-catalysed cyclization of amino allylic carbonates containing chiral protecting group with known and specified absolute configuration. Using a methylbenzylamine-derived auxiliary, piperidine cyclization products can be accessed as single stereoisomers. Other auxiliaries derived from amino acids afforded moderate diastereomeric ratios of up to 23:77. Taking into account the obtained results and the literature data, we assume that in each of these cases the sense of asymmetric induction was the same and the major isomer coresponded to (2*S*)-**7** rather than (2*R*)-**6**. Moreover, the N-chiral protecting group affect the stereochemical result of the reaction, and the steric hindrance of the N-substituent determines the ratio of the formed diastereoisomers.

Experimental Section

General. All solvents and reagents were purchased from Sigma-Aldrich and were used as supplied, without additional purification. NMR spectra were recorded in $CDCl_3$ on Bruker Avance III (600 MHz for ^{1}H NMR, 150 MHz for ^{13}C NMR), coupling constants are reported in Hz. Chromatographic purification of compounds was achieved with 230-400 mesh size silica gel. The progress of reactions was monitored by silica gel thin layer chromatography plates (Merck TLC Silicagel 60 F_{254}).

Typical procedure for the synthesis of aminocarbonates 5a,b

1.5 M solution *i*-Pr_2NEt in DMF (2.4 mL *i*-Pr_2NEt in 6.7 mL DMF) and the corresponding amine: (*S*)-1-phenylethanamine and (*R*)-1-phenylethanamine (15.0 mmol) were added successively to a 0.8 M solution of bromide **4a-b** (5.0 mmol) in DMF (6.4 mL). The reaction mixture was stirred at room temperature until the transformation of the bromide was complete (16-24 h), as indicated by thin layer chromatography. After being diluted with EtOAc (30 mL), the mixture was then washed with H_2O (3 × 20 mL) and a saturated aqueous solution of NaCl (20 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel to give the allylic aminocarbonates **5a,b**.

(*S*,*E*)-Isobutyl {7-[(1-phenylethyl)amino]hept-2-en-1-yl} carbonate (**5a**). Colorless oil, 1.10 g, 66% yield; R_f (EtOAc/MeOH, 7 : 1) 0.54; $[\alpha]_D^{20}$ +27.4 (*c* 0.5, $CHCl_3$); ν_{max} (liquid film) 3323, 3079, 3052, 2961, 2933, 2879, 2865, 1740, 1670, 1513, 1496, 1473, 1452, 1248 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 0.94 (d, 6H, *J* 6.7, $CH_2CH(CH_3)_2$), 1.35-1.40 (m, 6H, CH_3, H-5, NH), 1.44-1.51 (m, 2H, H-6), 1.93-1.98 (m, 1H, $CH_2CH(CH_3)_2$), 2.02 (q, 2H, *J* 7.3, H-4), 2.39-2.43 (m, 1H, H-7), 2.48-2.52 (m, 1H, H-7), 3.76 (q, 1H, *J* 6.6, CHC_6H_5), 3.90 (d, 2H, *J* 6.7, $CH_2CH(CH_3)_2$), 4.54

(d, 2H, *J* 6.5, H-1), 5.56 (dtt, 1H, *J* 15.3, 6.5, 1.3, H-2), 5.74-5.79 (m, 1H, H-3), 7.21-7.25 (m, 1H, C_6H_5), 7.29-7.34 (m, 4H, C_6H_5); δ_C (150 MHz, $CDCl_3$) δ 18.9 ($CH_2CH(CH_3)_2$), 24.2 (CH_3), 26.5 ($CH_2CH(CH_3)_2$), 27.8 (C-4), 29.6 (C-5), 32.0 (C-6), 47.5 (C-7), 58.4 (CHC_6H_5), 68.4 (C-1), 74.0 ($CH_2CH(CH_3)_2$), 123.6 (C-2), 126.6, 127.0, 128.4 (C_6H_5), 136.9 (C-3), 145.5 (C_q), 155.2 (CO); MS-EI m/z: 334 (MH^+, 100); HRMS (EI): M^+, found 333.2304. $C_{20}H_{31}NO_3$ requires 333.2312.

(*R*,*E*)-Isobutyl {7-[(1-phenylethyl)amino]hept-2-en-1-yl} carbonate (**5b**)**.** Colorless oil, 0.68 g, 41% yield; R_f (EtOAc/MeOH, 7 : 1) 0.53; $[\alpha]_D^{20}$ -27.8 (*c* 0.5, $CHCl_3$); ν_{max} (liquid film) 3326, 3080, 3058, 3036, 2958, 2930, 2879, 2868, 1742, 1672, 1515, 1496, 1470, 1454, 1249 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 0.95 (d, 6H, *J* 6.8 $CH_2CH(CH_3)_2$), 1.34 (d, 3H, *J* 6.6 CH_3), 1.37-1.49 (m, 5H, H-5, H-6, NH), 1.93-2.00 (m, 1H, $CH_2CH(CH_3)_2$), 2.02 (q, 2H, *J* 7.1, H-4), 2.39-2.43 (m, 1H, H-7), 2.47-2.51 (m, 1H, H-7), 3.75 (q, 1H, *J* 6.6, CHC_6H_5), 3.91 (d, 2H, *J* 6.7, $CH_2CH(CH_3)_2$), 4.54 (d, 2H, *J* 6.6, H-1), 5.56 (dtt, 1H, *J* 15.4, 6.6, 1.4, H-2), 5.77 (dtt, 1H, *J* 15.4, 6.7, 1.02, H-3), 7.21-7.24 (m, 1H, C_6H_5), 7.29-7.34 (m, 4H, C_6H_5); δ_C (150 MHz, $CDCl_3$) δ 18.8 ($CH_2CH(CH_3)_2$), 24.1 (CH_3-CH), 26.4 ($CH_2CH(CH_3)_2$), 27.7 (C-4), 29.5 (C-5), 31.9 (C-6), 47.4 (C-7), 58.3 (CHC_6H_5), 68.3 (C-1), 73.9 ($CH_2CH(CH_3)_2$), 123.5 (C-2), 126.5, 126.8, 128.3 (C_6H_5), 136.8 (C-3), 155.2 (CO); MS-EI m/z: 334 (MH^+, 100); found: C, 71.61; H, 9.18; N, 4.38. $C_{20}H_{31}NO_3$ requires C, 72.04; H, 9.37; N, 4.20%.

Typical procedure for the synthesis of aminocarbonate 5c-j

A solution of appropriate bromide **4a-b** (0.5 g, 1 equiv.), K_2CO_3 (2 equiv.), appropriate amino acid hydrochloride (3 equiv.) in CH_3CN (8 mL) was stirred at 40 °C for 4 d. Then the reaction mixture was cooled, diluted with water (20 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic phases were washed with brine, dried over Na_2SO_4 and evaporated under reduced pressure to give clear liquid. The crude product was purified by flash column chromatography on silica gel to give allylic aminocarbonate **5c-j**.

(*S*,*E*)-Methyl 2-({7-[(isobutoxycarbonyl)oxy}]hept-5-en-1-yl}amino)-3-phenylpropanoate (**5c**). Colorless oil, 0.29 g, 43% yield; R_f (hexane/EtOAc, 3 : 1) 0.53; $[\alpha]_D^{20}$ +13.7 (*c* 0.5, $CHCl_3$); ν_{max} (liquid film) 3329, 3062, 3029, 2930, 2856, 1740, 1674, 1605, 1496, 1456, 1251 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 0.94 (d, 6H, *J* 6.7, $CH_2CH(CH_3)_2$), 1.33-1.39 (m, 2H, H-5), 1.40-1.48 (m, 2H, H-6), 1.53 (s, 1H, NH), 1.93-2.00 (m, 1H, $CH_2CH(CH_3)_2$), 2.03 (q, 2H, *J* 7.1, H-4), 2.41-2.48 (m, 1H, H-7), 2.54-2.61 (m, 1H, H-7), 2.95 (d, 2H, *J* 7.0, $CH_2C_6H_5$), 3.50 (t, 1H, *J* 7.2, NH*CH*), 3.64 (s, 3H, $COOCH_3$), 3.92 (d, 2H, *J* 6.7, $CH_2CH(CH_3)_2$), 4.56 (d, 2H, *J* 6.7, H-1), 5.58 (dt, 1H, *J* 15.4, 6.3, H-3), 5.77 (dt, 1H, *J* 15.4, 6.7, H-2), 7.10-7.33 (m, 5H, C_6H_5); δ_C (150 MHz, $CDCl_3$) δ 19.0 ($CH_2CH(CH_3)_2$), 26.4 (C-5), 27.9 (C-6), 29.6 ($CH_2CH(CH_3)_2$), 32.0 (C-4), 39.8 ($CH_2C_6H_5$), 48.0 (C-7), 51.6 ($COOCH_3$), 63.2 (NH*C*H), 68.5 (C-1), 74.1 ($CH_2CH(CH_3)_2$), 123.7 (C-2), 126.8, 128.5, 129.2, 136.9 (C_6H_5), 137.5 (C-3), 155.3 (CO), 175.2 (CO); found: C, 67.51; H, 8.76; N, 3.59. $C_{22}H_{33}NO_5$ requires C, 67.49; H, 8.50; N, 3.58%.

(*S*,*E*)-Methyl 2-({6-[(isobutoxycarbonyl)oxy]hex-4-en-1-yl}amino)-3-phenylpropanoate (**5d**)**.** Colorless oil, 0.32 g, 48% yield; R_f (hexane/EtOAc, 3 : 1) 0.51; $[\alpha]_D^{20}$ -6.4 (*c* 0.5, $CHCl_3$); ν_{max} (liquid film) 3327, 3029, 2955, 2875, 1740, 1670, 1605, 1497, 1456, 1254 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 0.87 (d, 6H, *J* 6.7, $CH_2CH(CH_3)_2$), 1.38-1.50 (m, 2H, H-5), 1.59 (s, 1H, NH), 1.85-1.92 (m, 1H, $CH_2CH(CH_3)_2$), 1.96 (q, 2H, *J* 6.8, H-4), 2.34-2.41 (m, 1H, H-6), 2.47-2.55 (m, 1H, H-6), 2.85 (d, 2H, *J* 6.9, $CH_2C_6H_5$), 3.41 (t, 1H, *J* 6.9, NH*CH*), 3.55 (s, 3H, $COOCH_3$), 3.83 (d, 2H, *J* 6.6, $CH_2CH(CH_3)_2$), 4.46 (d, 2H, *J* 6.6, H-1), 5.48 (dt, 1H, *J* 15.5, 6.5, H-3), 5.68 (dt, 1H, *J* 15.5, 6.6, H-2), 7.00-7.25 (m, 5H, C_6H_5); δ_C (150 MHz, $CDCl_3$) δ 19.1 ($CH_2CH(CH_3)_2$), 26.5 (C-4), 27.9 (C-5), 29.6 ($CH_2CH(CH_3)_2$), 39.9 ($CH_2C_5H_4$), 48.1 (C-6), 51.7 ($COOCH_3$), 63.3 (NH*C*H), 68.5 (C-1), 74.2 ($CH_2CH(CH_3)_2$), 123.8 (C-2), 126.8, 128.6, 129.3, 137.5 (C_6H_5), 136.9 (C-3), 155.4 (CO), 175.2 (CO); found: C, 67.09; H, 8.52; N, 3.52. $C_{21}H_{31}NO_5$ requires C, 66.82; H, 8.28; N, 3.71%.

(*S*,*E*)-Methyl 2-({6-[(isobutoxycarbonyl)oxy]hex-4-en-1-yl}amino)propanoate (**5e**). Colorless oil, 0.18 g, 34% yield; R_f (hexane/EtOAc, 3 : 1) 0.44; $[\alpha]_D^{20}$ -12.5 (*c* 1, $CHCl_3$); ν_{max} (liquid film) 3329, 2960, 2865, 1747, 1674, 1254 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 0.88 (d, 6H, *J* 6.7, $CH_2CH(CH_3)_2$), 1.23 (d, 3H, *J* 7.0, $CHCH_3$), 1.48-1.54 (m, 2H, H-

5), 1.56 (s, 1H, N*H*), 1.87-1.93 (m, 1H, $CH_2CH(CH_3)_2$), 2.05 (q, 2H, *J* 7.0, H-4), 2.40-2.44 (m, 1H, H-6), 2.50-2.55 (m, 1H, H-6), 3.25-3.29 (m, 1H, NHC*H*CH_3), 3.65 (s, 3H, COOC*H*$_3$), 3.85 (d, 2H, *J* 6.7, C*H*$_2$CH$(CH_3)_2$), 4.49 (d, 2H, *J* 6.4, H-1), 5.51-5.57 (m, 1H, H-3), 5.71-5.77 (m, 1H, H-2); δ_C (150 MHz, $CDCl_3$) δ 19.0 ($CH_2CH(CH_3)_2$), 19.1 ($CH_2CH(CH_3)_2$), 27.9 ($CH_2CH(CH_3)_2$), 29.4 (C-4), 30.0 (C-5), 47.5 (C-6), 51.8 ($COOCH_3$), 56.7 (NH*C*HCH_3), 68.4 (C-1), 74.0 ($CH_2CH(CH_3)_2$), 124.0 (C-2), 136.5 (C-3), 155.3 (CO), 176.3 (CO); found: C, 59.62; H, 9.16; N, 4.68. $C_{15}H_{27}NO_5$ requires C, 59.78; H, 9.03; N, 4.65%.

(*S*,*E*)-Methyl 2-({7-[(isobutoxycarbonyl)oxy]hept-5-en-1-yl}amino)propanoate (**5f**). Colorless oil, 0.34 g, 63% yield; R_f (hexane/EtOAc, 3 : 1) 0.34; $[\alpha]_D^{20}$ -14.0 (*c* 1, $CHCl_3$); ν_{max} (liquid film) 3329, 2965, 2875, 2791, 1747, 1670, 1261 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 0.90 (d, 6H, *J* 6.7, $CH_2CH(CH_3)_2$), 1.24 (d, 3H, *J* 7.0, CHC*H*$_3$), 1.33-1.47(m, 4H, H-5, H-6), 1.58 (s, 1H, N*H*), 1.88-1.95 (m, 1H, $CH_2CH(CH_3)_2$), 2.02 (q, 2H, *J* 7.0, H-4), 2.40-2.42 (m, 1H, H-7), 2.49-2.54 (m, 1H, H-7), 3.26-3.31 (m, 1H, NH*C*HCH_3), 3.67 (s, 3H, COOC*H*$_3$), 3.86 (d, 2H, *J* 6.7, C*H*$_2$CH$(CH_3)_2$), 4.50 (d, 2H, *J* 6.4, H-1), 5.52-5.57 (m, 1H, H-3), 5.72-5.77 (m, 1H, H-2); δ_C (150 MHz, $CDCl_3$) δ 19.0 ($CH_2CH(CH_3)_2$), 19.2 ($CH_2CH(CH_3)_2$), 26.6 ($CH_2CH(CH_3)_2$), 27.9 (C-5), 29.8 (C-4), 32.1 (C-6), 47.9 (C-7), 51.8 ($COOCH_3$), 56.8 (NH*C*HCH_3), 68.5 (C-1), 74.2 ($CH_2CH(CH_3)_2$), 123.8 (C-2), 136.9 (C-3), 155.4 (CO), 176.4 (CO); found: C, 60.98; H, 9.21; N, 4.45. $C_{16}H_{29}NO_5$ requires C, 60.93; H, 9.27; N, 4.44%.

(*S*,*E*)-Methyl 2-({6-[(isobutoxycarbonyl)oxy]hex-4-en-1-yl}amino)-4-methylpentanoate (**5g**). Colorless oil, 0.23 g, 38% yield; R_f (hexane/EtOAc, 3 : 1) 0.49; $[\alpha]_D^{20}$ -6.6 (*c* 0.5, $CHCl_3$); ν_{max} (liquid film) 3329, 2957, 2872, 1740, 1670, 1252 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 0.86 (d, 3H, *J* 6.6, $CHCH_2CH(CH_3)_2$), 0.88 (d, 3H, *J* 6.6, $CHCH_2CH(CH_3)_2$), 0.91 (d, 6H, *J* 6.7, $CH_2CH(CH_3)_2$), 1.39-1.43 (m, 2H, H-5), 1.47-1.55 (m, 2H, CHC*H*$_2$CH$(CH_3)_2$), 1.64-1.70 (m, 2H, N*H*, $CHCH_2CH(CH_3)_2$), 1.90-1.96 (m, 1H, $CH_2CH(CH_3)_2$), 2.06 (q, 2H, *J* 7.2, H-4), 2.37-2.41 (m, 1H, H-6), 2.52-2.56 (m, 1H, H-6), 3.21 (t, 1H, *J* 7.3, C*H*NH), 3.67 (s, 3H, COOC*H*$_3$), 3.87 (d, 2H, *J* 6.6, C*H*$_2$CH$(CH_3)_2$), 4.52 (d, 2H, *J* 6.4, H-1), 5.56 (dt, 1H, *J* 15.4, 6.5, H-3), 5.76 (dt, 1H, *J* 15.4, 6.7, H-2); δ_C (150 MHz, $CDCl_3$) δ 19.0 and 19.0 ($CH_2CH(CH_3)_2$), 22.5 and 22.8 ($CHCH_2CH(CH_3)_2$), 25.1 ($CHCH_2CH(CH_3)_2$), 27.9 ($CH_2CH(CH_3)_2$), 29.4 (C-5), 30.0 (C-4), 43.0 ($CHCH_2CH(CH_3)_2$), 47.7 (C-6), 51.7 ($COOCH_3$), 60.2 (NH*C*H), 68.5 (C-1), 74.2 ($CH_2CH(CH_3)_2$), 123.9 (C-2), 136.6 (C-3), 155.4 (CO), 176.7 (CO); found: C, 63.11; H, 9.76; N, 3.89. $C_{18}H_{33}NO_5$ requires C, 62.95; H, 9.68; N, 4.08%.

(*S*,*E*)-Methyl 2-({7-[(isobutoxycarbonyl)oxy]hept-5-en-1-yl}amino)-4-methylpentanoate (**5h**). Colorless oil, 0.30 g, 50% yield; R_f (hexane/EtOAc, 3 : 1) 0.53; $[\alpha]_D^{20}$ -4.0 (*c* 0.5, $CHCl_3$); ν_{max} (liquid film) 3330, 2956, 2931, 2872, 1740, 1674, 1252 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 0.86 (d, 3H, *J* 6.6, $CHCH_2CH(CH_3)_2$), 0.89 (d, 3H, *J* 6.6, $CHCH_2CH(CH_3)_2$), 0.92 (d, 6H, *J* 6.7, $CH_2CH(CH_3)_2$), 1.36-1.45 (m, 6H, CHC*H*$_2$CH$(CH_3)_2$, H-5, H-6), 1.63-1.70 (m, 2H, N*H*, $CHCH_2CH(CH_3)_2$), 1.90-1.96 (m, 1H, $CH_2CH(CH_3)_2$), 2.03 (q, 2H, *J* 7.2, H-4), 2.37-2.42 (m, 1H, H-7), 2.50-2.55 (m, 1H, H-7), 3.22 (t, 1H, *J* 7.3, C*H*NH), 3.67 (s, 3H, COOC*H*$_3$), 3.88 (d, 2H, *J* 6.6, C*H*$_2$CH$(CH_3)_2$), 4.52 (d, 2H, *J* 6.5, H-1), 5.51-5.57 (m, 1H, H-3), 5.72-5.79 (m, 1H, H-2); δ_C (150 MHz, $CDCl_3$) δ 19.1 and 19.1 ($CH_2CH(CH_3)_2$), 22.5 and 22.8 ($CHCH_2CH(CH_3)_2$), 25.2 ($CHCH_2CH(CH_3)_2$), 26.6 ($CH_2CH(CH_3)_2$), 28.0 (C-5), 29.9 (C-6), 32.2 (C-4), 43.1 ($CHCH_2CH(CH_3)_2$), 48.2 (C-7), 51.7 ($COOCH_3$), 60.3 (NH*C*H), 68.6 (C-1), 74.2 ($CH_2CH(CH_3)_2$), 123.8 (C-2), 137.1 (C-3), 155.5 (CO), 176.8 (CO); found: C, 64.02; H, 10.03; N, 3.98. $C_{19}H_{35}NO_5$ requires C, 63.84; H, 9.87; N, 3.92%.

(*S*,*E*)-Methyl 2-({6-[(isobutoxycarbonyl)oxy]hex-4-en-1-yl}amino)-3-methylbutanoate (**5i**). Colorless oil, 0.18 g, 31% yield; R_f (hexane/EtOAc, 3 : 1) 0.42; $[\alpha]_D^{20}$ -8.0 (*c* 0.5, $CHCl_3$); ν_{max} (liquid film) 3329, 2932, 2856, 1741, 1670, 1250 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 0.92 (d, 3H, *J* 6.8, $CHCH(CH_3)_2$), 0.93 (d, 3H, *J* 6.8, $CHCH(CH_3)_2$), 0.94 (d, 6H, *J* 6.8, $CH_2CH(CH_3)_2$), 1.44 (s, 1H, N*H*), 1.50-1.60 (m, 2H, H-5), 1.84-1.91 (m, 1H, CHC*H*$(CH_3)_2$), 1.93-2.00 (m, 1H, $CH_2CH(CH_3)_2$), 2.11 (q, 2H, *J* 7.3, H-4), 2.39 (dt, 1H, *J* 11.2, 7.0, H-6), 2.659 (dt, 1H, *J* 11.2, 6.7, H-6), 2.94 (d, 1H, *J* 6.1, C*H*$CH(CH_3)_2$), 3.71 (s, 3H, COOC*H*$_3$), 3.91 (d, 2H, *J* 6.7, C*H*$_2$CH$(CH_3)_2$), 4.55 (d, 2H, *J* 6.5, H-1), 5.60 (dt, 1H, *J* 15.2, 6.5, H-3), 5.80 (dt, 1H, *J* 15.2, 6.7, H-2); δ_C (150 MHz, $CDCl_3$) δ 18.9, 19.0, 19.0, 19.3 (CH_3), 27.9

($CH_2CH(CH_3)_2$), 29.4 (C-5), 30.0 (C-4), 31.8 ($CHCH(CH_3)_2$), 48.1 (C-6), 51.4 ($COOCH_3$), 67.6 (NHCH), 68.5 (C-1), 74.1 ($CH_2CH(CH_3)_2$), 123.8 (C-2), 136.8 (C-3), 155.4 (CO), 176.0 (CO); found: C, 62.12; H, 9.61; N, 4.16. $C_{17}H_{31}NO_5$ requires C, 61.98; H, 9.48; N, 4.25%.

(*S*,*E*)-Methyl 2-({7-[(isobutoxycarbonyl)oxy]hept-5-en-1-yl}amino)-3-methylbutanoate (**5j**). Colorless oil, 0.12 g, 21% yield; R_f (hexane/EtOAc, 3 : 1) 0.41; $[\alpha]_D^{20}$ -0.18 (*c* 1, $CHCl_3$); ν_{max} (liquid film) 3328, 2931, 2856, 1741, 1673, 1250 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 0.92 (d, 3H, *J* 6.7, $CHCH(CH_3)_2$), 0.95 (d, 3H, *J* 6.7, $CHCH(CH_3)_2$), 0.97 (d, 6H, *J* 6.7, $CH_2CH(CH_3)_2$), 1.38-1.45 (m, 4H, H-5, H-6), 1.58 (s, 1H, NH), 1.83-1.92 (m, 1H, $CHCH(CH_3)_2$), 1.93-2.01 (m, 1H, $CH_2CH(CH_3)_2$), 2.07 (q, 2H, *J* 6.8, H-4), 2.40 (dt, 1H, *J* 11.2, 7.7, H-7), 2.57 (dt, 1H, *J* 11.2, 6.2, H-7), 2.97 (d, 1H, *J* 6.2, $CHCH(CH_3)_2$), 3.72 (s, 3H, $COOCH_3$), 3.91 (d, 2H, *J* 6.7, $CH_2CH(CH_3)_2$), 4.56 (d, 2H, *J* 6.3, H-1), 5.59 (dt, 1H, *J* 15.5, 6.6, H-3), 5.80 (dt, 1H, *J* 15.4, 6.7, H-2); δ_C (150 MHz, $CDCl_3$) δ 19.1, 19.1, 19.2, 19.3 (CH_3), 26.6 (C-5), 28.0 ($CH_2CH(CH_3)_2$), 29.8 (C-6), 31.8 ($CHCH(CH_3)_2$), 32.2 (C-4), 48.6 (C-7), 51.5 ($COOCH_3$), 67.7 (NHCH), 68.6 (C-1), 74.2 ($CH_2CH(CH_3)_2$), 123.7 (C-2), 137.1 (C-3), 155.4 (CO), 175.9 (CO); found: C, 62.77; H, 9.86; N, 4.12. $C_{18}H_{33}NO_5$ requires C, 62.95; H, 9.68; N, 4.08.

Typical procedure for the $Pd^{0/II}$-catalysed reaction

The catalytic system was prepared by stirring $Pd_2(dba)_3$ (22.9 mg, 0.025 mmol) or $[PdCl(C_3H_5)]_2$ (9.1 mg, 0.025 mmol) and the ligand (0.055 mmol or 0.11 mmol) in an appropriate anhydrous solvent (3 mL) for 0.5 h in a Schlenk tube under argon. This solution was added, under argon, to a Schlenk tube containing the unsaturated amino carbonate **5a-i** (1 mmol) in an appropriate anhydrous solvent (3 mL). The solution was stirred at 25 °C (0 °C or 60 °C). After 24 h, removal of the solvent followed by column chromatography gave the corresponding product **6a-i**.

(*S*)-1-((*S*)-1-Phenylethyl)-2-vinylpiperidine (**7a**). Colorless oil, 0.21 g, 99% yield; R_f (EtOAc/ MeOH 7 : 1) 0.92; $[\alpha]_D^{20}$ 40.27 (*c* 0.5, $CHCl_3$); ν_{max} (liquid film) 3081, 3061, 3027, 2970, 2932, 2854, 2876, 1603, 1600, 1577, 1494, 1450, 1447, 1186, 733, 698 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.24 (d, 3H, *J* 6.8, CH_3CH), 1.26-1.39 (m, 2H, H-4, H-5), 1.45-1.55 (m, 2H, H-3, H-5), 1.64-1.71 (m, 2H, H-3, H-4), 2.13 (dt, 1H, *J* 11.6, 2.0, H-6), 2.44 (dt, 1H, *J* 11.6, 3.9, H-6), 3.12 (dt, 1H, *J* 9.3, 2.6, H-2), 4.14 (q, 1H, *J* 6.6, CHC_6H_5), 5.07 (dd, 1H, *J* 10.2, 1.5, $CHCH_2$), 5.24 (dd, 1H, *J* 17.2, 1.5, $CHCH_2$), 5.93 (ddd, 1H, *J* 17.2, 10.2, 9.2, $CHCH_2$), 7.18 (t, 1H, *J* 7.3, C_6H_5), 7.31 (t, 2H, *J* 7.8, C_6H_5), 7.44 (d, 2H, *J* 7.8, C_6H_5); δ_C (50 MHz, $CDCl_3$) δ 10.2 (CH_3CH), 24.0 (C-4), 26.1 (C-5), 34.1 (C-3), 44.7 (C-6), 57.0 (CHPh), 63.0 (C-2), 114.9 ($CHCH_2$), 127.7, 127.8, 128.3, 128.3 (C_6H_5), 139.8 ($CHCH_2$); MS-EI m/z: 216 (MH^+, 100); HRMS (EI): M^+, found. 215.16709 $C_{15}H_{21}N$ requires 215.16740.

(*R*)-1-((*R*)-1-Phenylethyl)-2-vinylpiperidine (**6b**). Colorless oil, 0.20 g, 99% yield; R_f (EtOAc/MeOH 7 : 1) 0.92; $[\alpha]_D^{20}$ -42.56 (*c* 0.5, $CHCl_3$); ν_{max} (liquid film) 3081, 3060, 3022, 2950, 2911, 2871, 2850, 1611, 1580, 1490, 1450, 1439, 1182, 732, 690 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.26 (d, 3H, *J* 6.6, CH_3CH), 1.27-1.41 (m, 2H, H-4, H-5), 1.46-1.58 (m, 2H, H-3, H-5), 1.56-1.74 (m, 2H, H-3, H-4), 2.16 (dt, 1H, *J* 11.7. 2.8, H-6), 2.45 (dt, 1H, *J* 11.7, 4.2, H-6), 3.14 (dt, 1H, *J* 9.2. 2.8, H-2), 4.16 (q, 1H, *J* 6.7, CHC_6H_5), 5.09 (d, 1H, *J* 10.1, 1.0, $CHCH_2$), 5.25 (dd, 1H, *J* 17.3, 1.0, $CHCH_2$), 5.95 (ddd, 1H, *J* 17.3, 10.1, 9.1, $CHCH_2$), 7.22 (t, 1H, *J* 7.3, C_6H_5), 7.32 (t, 2H, *J* 7.6, C_6H_5), 7.46 (d, 2H, *J* 7.6, C_6H_5); δ_C (50 MHz, $CDCl_3$) δ 10.3 (CH_3CH), 24.0 (C-4), 26.2 (C-5), 34.2 (C-3), 44.8 (C-6), 57.1 (CHPh), 63.1 (C-2), 115.0 ($CHCH_2$), 126.3, 127.8, 128.5 (C_6H_5), 139.9 ($CHCH_2$); MS-EI m/z: 214.5 (MH^+, 100); HRMS (EI): M^+, found 215.16728. $C_{15}H_{21}N$ requires 215.16740.

(*S*)-Methyl 3-phenyl-2-((*R*)/(*S*)-2-vinylpiperidin-1-yl)propanoate (**6c/7c**). Colorless oil, 99% (THF, 25 °C), 99% (THF, 55 °C), 60% (THF, 0 °C), 99% (CH_2Cl_2, 25 °C) yield; ν_{max} (liquid film) 3056, 3022, 2936, 2857, 2809, 1739, 1622, 1600, 1499, 1451, 1435, 1261, 1119, 748, 726, 698 cm^{-1}; MS-EI m/z: 274 (MH^+, 100).

(*S*)-Methyl 3-phenyl-2-((*R*)-2-vinylpiperidin-1-yl)propanoate (**6c**). R_f (Hexane/EtOAc, 3 : 1) 0.83; $[\alpha]_D^{20}$ +5.93 (*c* 0.5, $CHCl_3$); δ_H (600 MHz, $CDCl_3$) 1.30-1.79 (m, 6H, 2H-3, 2H-4, 2H-5), 2.17 (dt, 1H, *J* 11.6, 2.6, H-6'), 2.86 (dd,

1H, *J* 13.6, 7.4, C*H*$_2$C$_6$H$_5$), 3.03 (dt, 1H, *J* 9.4, 2.6, H-6'), 3.08 (dd, 1H, *J* 13.4, 7.4, C*H*$_2$C$_6$H$_5$), 3.08–3.12 (m, 1H, H-2), 3.67 (s, 3H, OCH$_3$), 3.88 (t, 1H, *J* 7.5, C*H*C=O), 5.03 (dd, 1H, *J* 10.1, 1.9, CHC*H*$_2$), 5.15 (dd, 1H, *J* 17.2, 1.9, CHC*H*$_2$), 5.39 (ddd, 1H, *J* 17.2, 10.1, 8.9, C*H*CH$_2$), 7.19–7.23 (m, 2H, C$_6$*H*$_5$), R$_f$ 7.26–7.31 (m, 3H, C$_6$*H*$_5$); δ_C (150 MHz, CDCl$_3$) δ 23.1, 23.9 (C-4, C-5), 29.1 (C-3), 39.0 (*C*H$_2$C$_6$H$_5$), 46.7 (COO*C*H$_3$), 64.2 (C-6), 64.9 (C-2), 68.3 (*C*HC=O), 116.6 (CH*C*H$_2$), 126.2, 128.9, 129.0, 129.6, 131.0, 132.7 (*C*$_6$H$_5$), 141.6 (*C*HCH$_2$), 167.9 (C=O); HRMS (EI): M$^+$, found 273.17269. $C_{17}H_{23}NO_2$ requires 273.17288.

(*S*)-Methyl 3-phenyl-2-((*S*)-2-vinylpiperidin-1-yl)propanoate (**7c**). (Hexane/EtOAc, 3 : 1) 0.70; $[\alpha]_D^{20}$ -48.8 (*c* 0.5, CHCl$_3$); δ_H (600 MHz, CDCl$_3$) 1.30-1.79 (m, 6H, 2H-3, 2H-4, 2H-5), 2.47 (dt, 1H, *J* 11.3, 2.8, H-6'), 2.96 (dt, 1H, *J* 11.3, 2.8, H-6'), 2.99 (dd, 1H, *J* 13.1, 10.3, C*H*$_2$C$_6$H$_5$), 3.07–3.12 (m, 3H, C*H*$_2$C$_6$H$_5$, H-2), 3.59 (s, 3H, OC*H*$_3$), 3.91 (dd, 1H, *J* 10.3, 4.1, C*H*C=O), 5.18 (dd, 1H, *J* 10.2, 1.8, CHC*H*$_2$), 5.28 (dd,1H, *J* 17.3, 1.8, CHC*H*$_2$), 5.89 (ddd, 1H, *J* 17.3, 10.2, 9.0, C*H*CH$_2$), 7.14–7,20 (m, 3H, C$_6$*H*$_5$), 7.23–7.28 (m, 2H, C$_6$*H*$_5$); δ_C (150 MHz, CDCl$_3$) δ 23.1, 23.9 (C-4, C-5), 30.5 (C-3), 38.9 (*C*H$_2$C$_6$H$_5$), 47.2 (COO*C*H$_3$), 64.3 (C-6), 66.2 (C-2), 68.3 (*C*HC=O), 116.3 (CH*C*H$_2$), 126.2, 128.4, 129.0, 129.5, 131.0, 132.7 (*C*$_6$H$_5$), 141.5 (*C*HCH$_2$), 167.8 (C=O); HRMS (EI): M$^+$, found 273.17254. $C_{17}H_{23}NO_2$ requires 273.17288.

(*S*)-Methyl 3-phenyl-2-((*R*)/(*S*)-2-vinylpyrrolidin-1-yl)propanoate (**6d/7d**). Colorless oil, 99% (THF, 25 °C), 98% (CH$_2$Cl$_2$, 25 °C) yield; ν_{max} (liquid film) 3056, 3025, 2942, 2870, 1739, 1654, 1603, 1578, 1499, 1442, 1204, 1125, 751, 701 cm^{-1}; MS-EI m/z: 260 (MH$^+$, 100).

(*S*)-Methyl 3-phenyl-2-((*R*)-2-vinylpyrrolidin-1-yl)propanoate (**6d**). (Hexane/EtOAc, 3 : 1) 0.81; $[\alpha]_D^{20}$ -16.21 (*c* 0.5, CHCl$_3$); δ_H (600 MHz, CDCl$_3$) 1.25-1.78 (m, 4H, H-3, H-4), 2.13 (ddd, 1H, *J* 11.7, 9.4, 2.5, H-5), 2.82 (dd, 1H, *J* 13.4, 7.4, C*H*$_2$C$_6$H$_5$), 3.00 (ddd, 1H, *J* 9.4, 7.5, 3.0, H-5'), 3.05 (dd, 1H, *J* 13.4, 7.4, C*H*$_2$C$_6$H$_5$), 3.05–3.09 (m, 1H, H-2), 3.64 (s, 3H, OC*H*$_3$), 3.85 (t, 1H, *J* 7.5, C*H*C=O), 4.99 (dd, 1H, *J* 10.1, 1.9, CHC*H*$_2$), 5.12 (dd, 1H, *J* 17.5, 1.9, CHC*H*$_2$), 5.35 (ddd, 1H, *J* 17.5, 10.1, 8.8, C*H*CH$_2$), 7.15–7.20 (m, 2H, C$_6$*H*$_5$), 7.23–7.28 (m, 3H, C$_6$*H*$_5$); δ_C (150 MHz, CDCl$_3$) δ 23.9 (C-4), 29.1 (C-3), 38.9 (*C*H$_2$C$_6$H$_5$), 46.7 (COO*C*H$_3$), 50.9 (C-5), 62.5 (C-2), 68.3 (*C*HC=O), 116.6 (CH*C*H$_2$), 126.4, 128.3, 129.0, 129.2, 131.0, 140.7 (*C*$_6$H$_5$), 132.7 (*C*HCH$_2$), 167.9 (C=O); HRMS (EI): M$^+$, found 259.15708. $C_{16}H_{21}NO_2$ requires 259.15723.

(*S*)-Methyl 3-phenyl-2-((*S*)-2-vinylpyrrolidin-1-yl)propanoate (**7d**). (Hexane/EtOAc, 3 : 1) 0.65; $[\alpha]_D^{20}$ -8.13 (*c* 1, CHCl$_3$); δ_H (600 MHz, CDCl$_3$) 1.46-1.74 (m, 4H, H-3, H-4), 2.44 (ddd, 1H, *J* 2.8, 9.8, 7.5, H-5), 2.91 (ddd, 1H, *J* 4.0, 11.9, 9.8, H-5), 2.96 (dd, 1H, *J* 13.1, 10.3, C*H*$_2$C$_6$H$_5$), 3.03-3.08 (m, 2H, H-2, C*H*$_2$C$_6$H$_5$), 3.56 (s, 3H, OC*H*$_3$), 3.88 (dd, 1H, *J* 10.3, 4.1, C*H*C=O), 5.15 (dd, 1H, *J* 10.1, 1.8, CHC*H*$_2$), 5.24 (dd, 1H, *J* 17.5, 1.8, CHC*H*$_2$), 5.86 (ddd, 1H, *J* 17.5, 10.1, 9.0, C*H*CH$_2$), 7.12-7.17 (m, 1H, C$_6$*H*$_5$), 7.20-7.24 (m, 1H, C$_6$*H*$_5$), 7.30-7.44 (m, 3H, C$_6$*H*$_5$); δ_C (150 MHz, CDCl$_3$) 23.0 (C-4), 30.6 (C-3), 37.7 (*C*H$_2$C$_6$H$_5$), 46.7 (COO*C*H$_3$), 50.9 (C-5), 65.1 (C-2), 65.7 (*C*HC=O), 116.6 (CH*C*H$_2$), 128.3, 128.9, 129.0, 129.6, 131.0, 138.8 (*C*$_6$H$_5$), 132.6 (*C*HCH$_2$), 167.8 (C=O); HRMS (EI): M$^+$, found 259.15711. $C_{16}H_{21}NO_2$ requires 259.15723.

(*S*)-Methyl 2-((*R*)/(*S*)-2-vinylpyrrolidin-1-yl)propanoate (**6e/7e**). Colorless oil, 97% (THF, 55 °C), 98% (CH$_2$Cl$_2$, 35 °C) yield; ν_{max} (liquid film) 3053, 2965, 2873, 1733, 1651, 1261, 1192 cm^{-1}; MS-EI m/z: 184 (MH$^+$, 100); HRMS (EI): M$^+$, found 183.12591. $C_{10}H_{17}NO_2$ requires 183.12593.

(*S*)-Methyl 2-((*R*)-2-vinylpyrrolidin-1-yl)propanoate (**6e**). δ_H (600 MHz, CDCl$_3$) 1.26 (d, 3H, *J* 7.2, CHC*H*$_3$), 1.45-1.70 (m, 4H, H-3, H-4), 2.73 (q, 1H, *J* 8.5, H-5), 2.94-2.97 (m, 1H, H-5), 3.16 (q, 1H, *J* 7.9, H-2), 3.51 (q, 1H, *J* 7.2, C*H*CH$_3$), 3.59 (s, 3H, COOC*H*$_3$), 4.94 (dd, 1H, *J* 10.0, 1.9, CH=C*H*$_2$), 5.03 (dd, 1H, *J* 18.5, 1.9, CHC*H*$_2$), 5.56 (ddd, 1H, *J* 18.2, 10.0, 8.3, C*H*CH$_2$); δ_C (150 MHz, CDCl$_3$) δ 17.3 (CH*C*H$_3$), 22.8 (C-4), 32.2 (C-3), 46.8 (C-5), 51.0 (COO*C*H$_3$), 55.8 (*C*HCH$_3$), 65.8 (C-2), 116.4 (CH*C*H$_2$), 140.9 (*C*HCH$_2$), 174.1 (C=O).

(*S*)-Methyl 2-((*S*)-2-vinylpyrrolidin-1-yl)propanoate (**7e**). δ_H (600 MHz, CDCl$_3$) 1.18 (d, 3H, *J* 6.9, CHC*H*$_3$), 1.45-1.70 (m, 4H, H-3, H-4), 2.43 (q, 1H, *J* 8.5, H-5), 2.97-2.99 (m, 1H, H-5), 3.03 (q, 1H, *J* 7.8, H-2), 3.54 (q, 1H, *J* 6.9, C*H*CH$_3$), 3.60 (s, 3H, COOC*H*$_3$), 4.99 (dd, 1H, *J* 10.0, 1.9, CH=C*H*$_2$), 5.06 (dd, 1H, *J* 18.5, 1.9, CHC*H*$_2$), 5.64 (ddd,

1H, *J* 18.5, 10.0, 8.6, C*H*CH_2); δ_C (150 MHz, $CDCl_3$) 14.1 (CH*C*H_3), 22.5 (C-4), 32.1 (C-3), 49.4 (C-5), 51.6 (COO*C*H_3), 58.9 (*C*HCH_3), 64.9 (C-2), 115.7 (CH*C*H_2), 141.2 (*C*HCH_2), 174.9 (C=O).

(*S*)-Methyl 2-((*R*)/(*S*)-2-vinylpiperidin-1-yl)propanoate (**6f/7f**). Colorless oil, 99% (THF, 25 °C), 99% (CH_2Cl_2, 25 °C) yield; ν_{max} (liquid film) 3060, 2958, 2927, 2854, 1736, 1654, 1258, 1122 cm^{-1}; MS-EI m/z: 198 (MH^+, 100); HRMS (EI): M^+, found 197.14155. $C_{11}H_{19}NO_2$ requires 197.14158.

(*S*)-Methyl 2-((*R*)-2-vinylpiperidin-1-yl)propanoate (**6f**). δ_H (600 MHz, $CDCl_3$) 1.19 (d, 3H, *J* 7.10, CHC*H*$_3$), 1.20-1.65 (m, 6H, H-3, H-4, H-5), 2.15-2.23 (m, 1H, H-6), 2.89 (d, 1H, *J* 11.2, H-6), 3.04 (dd, 1H, *J* 10.7, 2.5, H-2), 3.59 (s, 3H, COOC*H*$_3$), 3.70 (q, 1H, *J* 7.6, C*H*CH_3), 5.00 (dd, 1H, *J* 10.1, 1.8, CHC*H*$_2$), 5.12 (dd, 1H, *J* 17.2, 1.8, CHC*H*$_2$), 5.61 (ddd, 1H, *J* 17.2, 10.1, 9.6, C*H*CH_2); δ_C (150 MHz, $CDCl_3$) δ 19.0 (CH*C*H_3), 24.4 and 26.5 (C-4 and C-5), 34.3 (C-3), 45.9 (C-6), 50.8 (COO*C*H_3), 57.4 (*C*HCH_3), 64.8 (C-2), 116.6 (CH*C*H_2), 141.6 (*C*HCH_2), 173.7 (C=O).

(*S*)-Methyl 2-(*S*)-2-vinylpiperidin-1-yl)propanoate (**7f**). δ_H (600 MHz, $CDCl_3$) 1.06 (d, 3H, *J* 7.0, CHC*H*$_3$), 1.20-1.65 (m, 6H, H-3, H-4, H-5), 2.15-2.23 (m, 1H, H-6), 2.70 (dt, 1H, *J* 11.2, 3.1, H-6), 2.81 (ddd, 1H, *J* 10.7, 9.5, 3.1, H-2), 3.62 (s, 3H, COOC*H*$_3$), 3.72 (q, 1H, *J* 7.0, C*H*CH_3), 4.98 (dd, 1H, *J* 10.1, 1.7, CHC*H*$_2$), 5.09 (dd, 1H, *J* 17.1, 1.7, CHC*H*$_2$), 5.72 (ddd, 1H, *J* 17.1, 10.1, 1.9, C*H*CH_2); δ_C (150 MHz, $CDCl_3$) 16.1 (CH*C*H_3), 24.1 and 26.0 (C-4 and C-5), 33.7 (C-3), 47.0 (C-6), 51.9 (COO*C*H_3), 58.7 (*C*HCH_3), 63.8 (C-2), 116.1 (CH*C*H_2), 141.2 (*C*HCH_2), 174.8 (C=O).

(*S*)-Methyl 4-methyl-2-((*R*)/(*S*)-2-vinylpyrrolidin-1-yl)pentanoate (**6g/7g**). Colorless oil, 98% (THF, 25 °C), 97% (CH_2Cl_2, 25 °C) yield; ν_{max} (liquid film) 3053, 2952, 2923, 2873, 1733, 1651, 1195, 1122 cm^{-1}; MS-EI m/z: 226 (MH^+, 100); HRMS (EI): M^+, found 225.17282. $C_{13}H_{23}NO_2$ requires 225.17288.

(*S*)-Methyl 4-methyl-2-((*R*)-2-vinylpyrrolidin-1-yl)pentanoate (**6g**). δ_H (600 MHz, $CDCl_3$) 0.79 (d, 3H, *J* 6.7, $CHCH_2CH(CH_3)_2$), 0.83 (d, 3H, *J* 6.7, $CHCH_2CH(CH_3)_2$), 1.30-1.90 (m, 7H, H-3, H-4, $CHCH_2CH(CH_3)_2$), 2.77 (q, 1H, *J* 8.2, H-5), 2.88 (ddd, 1H, *J* 8.6, 8.6, 5.0, H-5), 3.07 (q, 1H, *J* 7.9, H-2), 3.45 (dd, 1H, *J* 8.7, 6.7, $CHCH_2CH(CH_3)_2$), 3.60 (s, 3H, COOC*H*$_3$), 5.01 (dd, 1H, *J* 10.0, 1.8, CHC*H*$_2$), 5.06 (dd, 1H, *J* 17.4, 1.6, CHC*H*$_2$), 5.52 (ddd, 1H, *J* 17.4, 10.0, 8.6, C*H*CH_2); δ_C (150 MHz, $CDCl_3$) δ 22.1 ($CHCH_2CH(CH_3)_2$), 23.1 (C-4), 24.9 ($CHCH_2CH(CH_3)_2$), 32.3 (C-3), 40.2 ($CHCH_2CH(CH_3)_2$), 46.1 (C-5), 50.8 (COO*C*H_3), 58.3 ($CHCH_2CH(CH_3)_2$), 65.0 (C-2), 116.5 (CH*C*H_2), 141.8 (*C*HCH_2), 174.3 (C=O).

(*S*)-Methyl 4-methyl-2-((*S*)-2-vinylpyrrolidin-1-yl)pentanoate (**7g**). δ_H (600 MHz, $CDCl_3$) 0.81 (d, 3H, *J* 6.9, $CHCH_2CH(CH_3)_2$), 0.82 (d, 3H, *J* 6.9, $CHCH_2CH(CH_3)_2$), 1.30-1.90 (m, 7H, H-3, H-4, $CHCH_2CH(CH_3)_2$), 2.49 (q, 1H, *J* 8.5, H-5), 2.99 (ddd, 1H, *J* 8.3, 8.3, 3.4, H-5), 3.17 (q, 1H, *J* 7.7, H-2), 3.32 (dd, 1H, *J* 9.8, 5.0, $CHCH_2CH(CH_3)_2$), 3.59 (s, 3H, COOC*H*$_3$), 4.92 (dd, 1H, *J* 10.1, 1.4, CHC*H*$_2$), 5.00 (dd, 1H, *J* 17.3, 1.0, CHC*H*$_2$), 5.63 (ddd, 1H, *J* 17.3, 10.1, 9.1, C*H*CH_2); δ_C (150 MHz, $CDCl_3$) 22.2 ($CHCH_2CH(CH_3)_2$), 23.0 (C-4), 25.4 ($CHCH_2CH(CH_3)_2$), 32.3 (C-3), 37.9 ($CHCH_2CH(CH_3)_2$), 50.2 (C-5), 51.3 (COO*C*H_3), 62.2 ($CHCH_2CH(CH_3)_2$), 65.0 (C-2), 115.2 (CH*C*H_2), 143.5 (*C*HCH_2), 174.4 (C=O).

(*S*)-Methyl 4-methyl-2-((*R*)/(*S*)-2-vinylpiperidin-1-yl)pentanoate (**6h/7h**). Colorless oil, 98% (THF, 55 °C), 98% (CH_2Cl_2, 35 °C) yield; ν_{max} (liquid film) 3056, 2961, 2936, 2873, 1739, 1261, 1097 cm^{-1}; MS-EI m/z: 240 (MH^+, 100); HRMS (EI): M^+, found 239.18847. $C_{14}H_{25}NO_2$ requires 239.18843.

(*S*)-Methyl 4-methyl-2-((*R*)-2-vinylpiperidin-1-yl)pentanoate (**6h**)**.** δ_H (600 MHz, $CDCl_3$) 0.73 (d, 3H, *J* 6.6, $CHCH_2CH(CH_3)_2$), 0.82 (d, 3H, *J* 6.6, $CHCH_2CH(CH_3)_2$), 1.30-1.90 (m, 9H, H-3, H-4, H-5, $CHCH_2CH(CH_3)_2$), 2.09 (ddd, 1H, *J* 11.8, 11.2, 2.3, H-6), 2.86-2.98 (m, 2H, H-2, H-6), 3.57 (s, 3H, COOC*H*$_3$), 3.61 (dd, 1H, *J* 9.8, 6.7, $CHCH_2CH(CH_3)_2$), 5.01 (dd, 1H, *J* 10.0, 1.5, CHC*H*$_2$), 5.10 (dd, 1H, *J* 17.2, 1.6, CHC*H*$_2$), 5.54 (ddd, 1H, *J* 17.2, 10.0, 9.3, C*H*CH_2); δ_C (150 MHz, $CDCl_3$) δ 22.2 ($CHCH_2CH(CH_3)_2$), 23.7, 24.0 (C-4 and C-5), 26.2 ($CHCH_2CH(CH_3)_2$), 34.0 (C-3), 39.0 ($CHCH_2CH(CH_3)_2$), 46.6 (C-6), 51.6 (COO*C*H_3), 65.7 ($CHCH_2CH(CH_3)_2$), 68.3 (C-2), 116.0 (CH*C*H_2), 140.0 (*C*HCH_2), 174.4 (C=O).

(*S*)-Methyl 4-methyl-2-((*S*)-2-vinylpiperidin-1-yl)pentanoate (**7h**)**.** δ_H (600 MHz, $CDCl_3$) 0.78 (d, 3H, *J* 6.6, $CHCH_2CH(CH_3)_2$), 0.85 (d, 3H, *J* 6.6, $CHCH_2CH(CH_3)_2$), 1.25-1.70 (m, 9H, H-3, H-4, H-5, $CHCH_2CH(CH_3)_2$), 2.27

(ddd, 1H, *J* 11.6, 11.0, 2.9, H-6), 2.83 (dt, 1H, *J* 11.6, 2.9, H-6), 2.86-2.98 (m, 1H, H-2), 3.55 (dd, 1H, *J* 10.4, 4.0, C*H*$CH_2CH(CH_3)_2$), 3.61 (s, 3H, COOC*H*$_3$), 5.00 (dd, 1H, *J* 10.4, 1.5, CHC*H*$_2$), 5.05 (dd, 1H, *J* 17.3, 1.0, CHC*H*$_2$), 5.78 (ddd, 1H, *J* 17.3, 10.4, 9.4, C*H*CH_2); δ_C (150 MHz, $CDCl_3$) 22.2 ($CHCH_2CH(CH_3)_2$), 23.6, 23.7 (C-4 and C-5), 25.8 ($CHCH_2CH(CH_3)_2$), 33.4 (C-3), 39.0 ($CHCH_2CH(CH_3)_2$), 46.6 (C-6), 51.6 (COOCH_3), 62.2 ($CHCH_2CH(CH_3)_2$), 64.2 (C-2), 116.0 (CHCH_2), 141.3 (CHCH_2), 174.4 (C=O).

(*S*)-Methyl 3-methyl-2-((*R*)/(*S*)-2-vinylpyrrolidin-1-yl)butanoate (**6i/7i**). Colorless oil, 99% (THF, 25 °C) yield; ν_{max} (liquid film) 3060, 2958, 2926, 2870, 1731, 1621, 1267, 1194 cm^{-1}; MS-EI m/z: 212 (MH^+, 100); HRMS (EI): M^+, found 211.15715. $C_{12}H_{21}NO_2$ requires 211.15723.

(*S*)-Methyl 3-methyl-2-((*R*)-2-vinylpyrrolidin-1-yl)butanoate (**6i**). δ_H (600 MHz, $CDCl_3$) 0.85 (d, 3H, *J* 6.6, CHCH(C*H*$_3$)$_2$), 0.96 (d, 3H, *J* 6.6, CHCH(C*H*$_3$)$_2$), 1.88-1.95 (m, 2H, H-3), 1.75-1.83 (m, 2H, H-4), 2.08-2.16 (m, 1H, CHC*H*$(CH_3)_2$), 2.80 (q, 1H, *J* 8.2, H-5), 2.92 (ddd, 1H, *J* 8.2, 7.9, 4.3, H-5), 2.89-3.10 (m, 2H, H-2, C*H*$CH(CH_3)_2$), 3.67 (s, 3H, COOC*H*$_3$), 5.08 (dd, 1H, *J* 10.0, 1.8, CHC*H*$_2$), 5.15 (dd, 1H, *J* 17.0, 1.6, CHC*H*$_2$), 5.56 (ddd, 1H, *J* 17.0, 10.0, 8.2, C*H*CH_2); δ_C (150 MHz, $CDCl_3$) δ 19.0 (CHCH(*C*H$_3$)$_2$), 23.0 (C-4), 28.8 (CH*C*H$(CH_3)_2$), 31.0 (C-3), 50.8 (COO*C*H$_3$), 45.9 (C-5), 64.9 (*C*HCH$(CH_3)_2$), 67.5 (C-2), 116.0 (CH*C*H$_2$), 143.5 (*C*HCH_2), 172.2 (C=O).

(*S*)-Methyl 3-methyl-2-((*S*)-2-vinylpyrrolidin-1-yl)butanoate (**7i**). δ_H (600 MHz, $CDCl_3$) 0.88 (d, 3H, *J* 6.7, CHCH(C*H*$_3$)$_2$), 0.95 (d, 3H, *J* 6.7, CHCH(C*H*$_3$)$_2$), 1.50-1.60 (m, 2H, H-3), 1.63-1.74 (m, 2H, H-4), 2.08-2.16 (m, 1H, CHC*H*$(CH_3)_2$), 2.62 (q, 1H, *J* 8.4, H-5), 2.89-3.10 (m, 1H, H-2), 3.08 (ddd, 1H, *J* 8.4, 8.2, 3.6, H-5), 3.38 (dd, 1H, *J* 8.1, 7.9, C*H*$CH(CH_3)_2$), 3.65 (s, 3H, COOC*H*$_3$), 4.94 (dd, 1H, *J* 10.0, 1.6, CHC*H*$_2$), 5.06 (dd, 1H, *J* 17.4, 1.1, CHC*H*$_2$), 5.71 (ddd, 1H, *J* 17.4, 10.0, 8.7, C*H*CH_2); δ_C (150 MHz, $CDCl_3$) 20.4 (CHCH(*C*H$_3$)$_2$), 23.0 (C-4), 31.5 (CH*C*H$(CH_3)_2$), 32.6 (C-3), 50.4 (COO*C*H_3), 50.8 (C-5), 65.1 (*C*HCH$(CH_3)_2$), 70.7 (C-2), 114.4 (CH*C*H_2), 142.0 (*C*HCH_2), 173.5 (C=O).

(*S*)-Methyl 3-methyl-2-((*R*)/(*S*)-2-vinylpiperidin-1-yl)butanoate (**6j/7j**). Colorless oil, 98% (THF, 25 °C) yield; ν_{max} (liquid film) 3060, 2961, 2930, 2873, 1733, 1622, 1268, 1192 cm^{-1}; MS-EI *m/z*: 226 (MH^+, 100); HRMS (EI): M^+, found 225.17279. $C_{13}H_{23}NO_2$ requires 225.17288.

(*S*)-Methyl 3-methyl-2-((*R*)-2-vinylpiperidin-1-yl)butanoate (**6j**). cδ_H (600 MHz, $CDCl_3$) 0.85 (d, 3H, *J* 6.7, CHCH(C*H*$_3$)$_2$), 0.90 (d, 3H, *J* 6.7, CHCH(C*H*$_3$)$_2$), 1.30-1.90 (m, 6H, H-3, H-4, H-5), 1.90-2.10 (m, 1H, CHC*H*$(CH_3)_2$), 2.55-2.59 (m, 1H, H-6), 2.74-2.85 (m, 2H, H-2, H-6), 3.04 (d, 1H, *J* 7.6, C*H*$CH(CH_3)_2$), 3.53 (s, 3H, COOC*H*$_3$), 5.02 (dd, 1H, *J* 10.1, 1.7, CHC*H*$_2$), 5.11 (dd, 1H, *J* 18.8, 1.0, CHC*H*$_2$), 5.52 (ddd, 1H, *J* 18.8, 10.1, 8.9, C*H*CH_2); δ_C (150 MHz, $CDCl_3$) δ 19.8 (CHCH(*C*H$_3$)$_2$), 26.5, 27.9 (C-4, C-5), 31.5 (CH*C*H$(CH_3)_2$), 33.8 (C-3), 44.3 (C-6), 52.2 (COO*C*H_3), 64.8 (C-2), 71.7 (*C*HCH$(CH_3)_2$), 115.7 (CH*C*H_2), 143.5 (*C*HCH_2), 177.5 (C=O).

(*S*)-Methyl 3-methyl-2-((*S*)-2-vinylpiperidin-1-yl)butanoate (**7j**). δ_H (600 MHz, $CDCl_3$) 0.85 (d, 3H, *J* 6.7, CHCH(C*H*$_3$)$_2$), 0.90 (d, 3H, *J* 6.7, CHCH(C*H*$_3$)$_2$), 1.30-1.90 (m, 6H, H-3, H-4, H-5), 1.90-2.10 (m, 1H, CHC*H*$(CH_3)_2$), 2.55-2.59 (m, 1H, H-6), 2.91 (d, 1H, *J* 7.4, C*H*$CH(CH_3)_2$), 2.97 (ddd, 1H, *J* 11.7, 8.0, 3.5, H-6), 3.13-3.18 (m, 1H, H-2), 3.67 (s, 3H, COOC*H*$_3$), 4.99 (dd, 1H, *J* 10.3, 1.6, CHC*H*$_2$), 5.09 (dd, 1H, *J* 18.8, 1.7, CHC*H*$_2$), 5.96 (ddd, 1H, *J* 18.8, 10.3, 9.1, C*H*CH_2); δ_C (150 MHz, $CDCl_3$) δ 20.4 (CHCH(*C*H$_3$)$_2$), 26.7 (C-4), 27.9 (C-5), 28.2 (CH*C*H$(CH_3)_2$), 33.8 (C-3), 44.3 (C-6), 52.2 (COO*C*H_3), 64.8 (C-2), 71.6 (*C*HCH$(CH_3)_2$), 115.7 (CH*C*H_2), 142.3 (*C*HCH_2), 174.6 (C=O).

(-)-(2*R*)-2-Ethylpiperidine hydrochloride (**8**) **and (+)-(2*S*)-2-Ethylpiperidine hydrochloride** (**9**). A catalytic amount of $Pd(OH)_2/C$ (25 mol %) was added to a solution of the corresponding 1-(1-phenylethyl)-2-vinylpiperidine **7a** or **6b** (0.5 mmol) in dry MeOH (15 mL) and the mixture was stirred under H_2 (2.5 atm) for 15 h at rt. Then, the mixture was filtered through a short plug of Celite (eluent MeOH) and concentrated HCl (0.1 mL) was added to the solution and the mixture was stirred at rt for 1 h after which the solvent was removed *in vacuo* obtaining the piperidine **8**: colorless solid, 69 mg, 92% yield, $[\alpha]_D^{20}$ -1.38 (*c* 0.5, MeOH), lit.[48] $[\alpha]_D^{23}$ -1.42 (*c* 1.8, MeOH), lit.[49] $[\alpha]_D^{23}$ -1.2 (*c* 0.2, EtOH), m.p. 205-207 °C, lit.[48] m.p. 210-212 °C, lit.[49] m.p. 205-206 °C, and piperidine **9**: 66 mg, 88% yield, $[\alpha]_D^{20}$ +1.29 (*c* 0.5, MeOH), m.p. 206-207 °C; δ_H (600 MHz, $CDCl_3$) 1.05 (t, 3H, *J*

7.6), 1.40-1.50 (m, 1H), 1.61-1.70 (m, 1H), 1.75-1.87 (m, 2H), 1.89-2.01 (m, 3H), 2.02-2.11 (m, 1H), 2.81-2.92 (m, 2H), 3.44-3.51 (m, 1H), 9.06 (br.s, 1H), 9.39 (br. s, 1H). The spectroscopic data are in accordance with ref's 48, 49.

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Supplementary Material

Copies of ^{1}H and ^{13}C NMR spectra of the obtained compounds.

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