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Tetrahedron: *Asymmetry* 18 (2007) 424–434
Tetrahedron: *Asymmetry*

Asymmetric synthesis of di- and trisubstituted pyrrolidinones via zirconium-mediated intramolecular coupling of *N*-3-alkenyl carbamates

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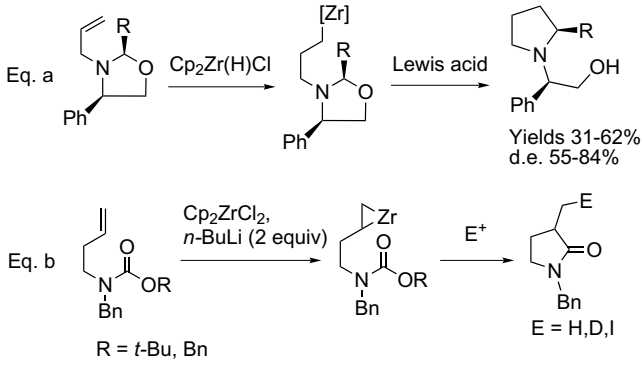
Received 2 January 2007; accepted 22 January 2007
Available online 21 February 2007

Abstract—*N*-3-Alkenyl carbamates, which are readily available in enantiomerically pure form, undergo a stereoselective intramolecular coupling under the effect of a Cp_2ZrCl_2/2*n*-BuLi reagent. The influence of the carbamate structure on the stereoselectivity was tested. The reaction gives an easy access to various di- and trisubstituted enantiopure pyrrolidinones.

1. Introduction

The pyrrolidine and pyrrolidinone moieties are present in many biologically active molecules, both naturally occurring and synthetic.[1] Therefore, the development of efficient and stereoselective methods for the synthesis of such nitrogen heterocycles is an important task. In addition to the C–N bond-forming cyclization reactions,[2] C–C bond-forming reactions have recently emerged as an interesting alternative for building five-membered nitrogen-heterocycles.[3] Among them, zirconium-mediated intramolecular coupling reactions[4] have been employed. We described a new diastereoselective synthesis of 2-substituted pyrrolidines from *N*-allyl oxazolidines via a tandem hydrozirconation–Lewis acid-mediated ring-closure sequence (Scheme 1, Eq. a).[5] Taguchi et al. found access to the pyrrolidinone ring system via a Zr(II)-mediated intramolecular coupling reaction starting from *N*-homoallyl carbamates (Scheme 1, Eq. b).[6] Interestingly, a possible functionalization of the pyrrolidinone side chain emphasizes the synthetic potential of this reaction.[7]

Although these two reactions employed the same strategy (i.e., the formal conversion of an alkene into a nucleophilic entity followed by a ring-closure step), the stereogenic centers are created at different stages. In contrast to the pyrrolidine synthesis, for which the configuration of the stereogenic center declined from the configuration of the aminal, the pyrrolidinone synthesis involves a C–Zr bond formation as the stereodetermining step. This offers the possibility of developing the asymmetric variant of the reaction. Herein, we report an efficient and diastereoselective zirconium-mediated synthesis of di- and trisubstituted pyrrolidinones (γ-lactams) from enantiomerically pure *N*-3-alkenyl carbamates.



Scheme 1. Access to pyrrolidines and pyrrolidinones via zirconium-mediated alkene activation.

2. Results and discussion

Since the required enantiomerically pure side chain can easily be obtained via diastereoselective allylation of amino

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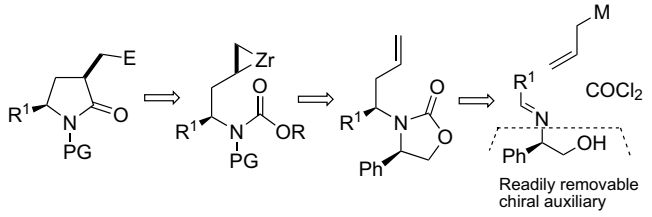
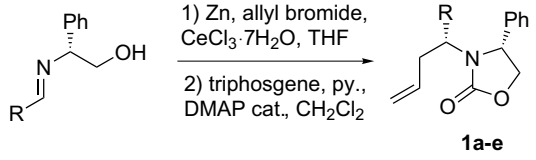
doi:10.1016/j.tetasy.2007.01.026

alcohol-derived imines, we first synthesized carbamates derived from phenylglycinol. In fact, an efficient final deprotection of such a chiral auxiliary is already known.[8] We also thought that the presence of an additional stereogenic center might influence the stereoselectivity of the cyclization (Scheme 2). Following this retrosynthetic approach, the pyrrolidinone skeleton results from zirconium-mediated intramolecular coupling reaction. The stereochemistry at the C3 atom in pyrrolidinone derives from the stereodefined zirconacyclopropane, which in turn is generated through the facial discrimination of the C=C double bond, under the effect of the proximal stereogenic centers (C1 and/or C2) of the nitrogen side chain of a carbamate. As indicated, such carbamates could be obtained simply.



Scheme 2. Retrosynthetic approach.

Carbamates **1a**–**e** were first prepared by employing readily available (*R*)-2-phenylglycinol. The reaction of phenylglycinol-derived imines with allylbromide and zinc in the presence of $CeCl_3{\cdot}7H_2O$ provided the corresponding amino alcohols in good yields, and in good to excellent diastereoselectivities.[9] Subsequent treatment with triphosgen, in the presence of pyridine and a catalytic amount of DMAP, gave the corresponding carbamates **1a**–**e** in almost quantitative yields[10] (Scheme 3).

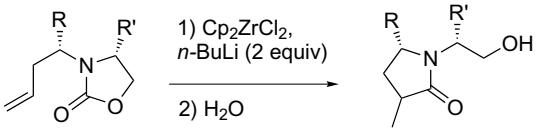


Scheme 3. Synthesis of carbamates **1a**–**e**.

These diversely substituted carbamates were submitted to the zirconium-mediated alkene–carbamate coupling reaction under modified Taguchi conditions (see Section 4). As shown in Table 1, the reaction proceeded smoothly with carbamates bearing aromatic (entries 1 and 4), heteroaromatic (entries 2 and 3), and alkyl R groups (entry 5) to afford the corresponding pyrrolidinones in good yields. However, a poor stereoselectivity (dr = 1.2:1–3:1) was observed in these reactions. The major diastereomer could be isolated in a pure form by column chromatography in most cases.

To estimate the influence of the carbamate substituent (R′ = Ph) upon the stereochemical outcome of the reaction, the same reaction sequence was applied to the substrates containing a substituent-free (R′ = H) ethanolamine-derived carbamate moiety (Table 1, entries 6–8).

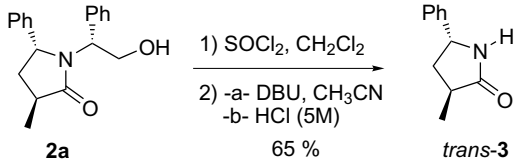
Table 1. Synthesis of disubstituted pyrrolidinones



Entry	R	R′	Compound	dr
1	Ph	Ph	**2a** (78%)	1.4:1
2	2-Fur	Ph	**2b** (75%)	1.2:1
3	2-(1-Me–Pyr)	Ph	**2c** (73%)	3:1
4	2-MeO–C_6H_4	Ph	**2d** (74%)	1.3:1
5	*i*-Pr	Ph	**2e** (78%)	1.4:1
6[a]	Ph	H	**2f** (78%)	2:1
7[a]	2-MeO–C_6H_4	H	**2g** (78%)	2:1
8[a]	Ph–CH=CH	H	**2h** (46%)	6:1

[a] Reaction carried out in the racemic series.

The diastereoselectivity was improved in these cases but remained moderate. Additionally, compound **2h** was obtained solely from carbamate **1h** bearing two alkene chains with a different degree of substitution (entry 8). As an example of deprotection, the chiral auxiliary was removed from diastereomerically pure **2a** to afford the corresponding enantiopure 3-methyl-5-phenylpyrrolidinone *trans*-**3** (Scheme 4).

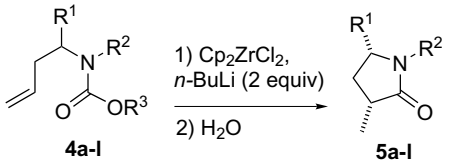


Scheme 4. Removal of the chiral auxiliary.

In a recent paper, Taguchi reported that a high level of diastereoselectivity could be achieved in the ester transfer coupling reaction using *t*-butyloxy *N*-tosyl carbamate. In contrast, no selectivity was obtained when employing the benzyloxy analogue.[7] We assumed that in our case, the low stereoselectivity originated from an inefficient discrimination of the carbonyl group, supposed to stereodirect the zirconocene approach. Therefore, a most suitable environment around the carbamate has been envisioned, by increasing the steric bulkiness at the O atom. This was ensured by using non-cyclic carbamates **4a**–**l** as starting materials (Table 2).

Accordingly, compounds **4a**–**l** were synthesized from the corresponding imines by alkylation and Boc protection. Compounds **4a**–**l** were subjected to the reaction conditions as previously described, and the results are shown in Table 2. The stereochemical outcome of the reaction has been demonstrated to depend strongly on the adjustment of the nitrogen- and oxygen-carbamate groups (R^2 and R^3). Whereas a total lack of diastereoselectivity was observed when combining two small or two large groups (entries 1–3), good diastereomeric ratios, in favor of the *cis*-isomer,[11] were obtained when combining a small and a large

Table 2. Synthesis of disubstituted carbamates **5**



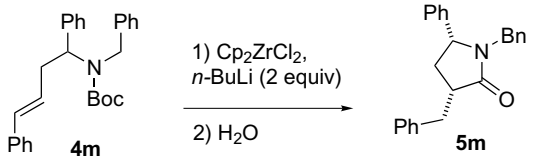
4a-l **5a-l**

Entry	R^1	R^2	R^3	Compound	dr
1[a]	Ph	PMP	^{t}Bu	**5a** (72%)	1.2:1
2[a]	Ph	Bn	Et	**5b** (67%)	1:1
3[a]	Ph	Bn	Bn	**5b** (68%)	1.2:1
4[a]	Ph	^{n}Pr	^{t}Bu	**5d** (71%)	8:1
5[a]	Ph	Bn	^{t}Bu	**5b** (72%)	7.5:1
6[a]	Ph	PMB	^{t}Bu	**5f** (69%)	7:1
7[a]	4-MeO–C_6H_4	Bn	^{t}Bu	**5g** (70%)	8:1
8[a]	2-MeO–C_6H_4	PMB	^{t}Bu	**5h** (68%)	5.6:1
9[a]	2-Furyl	Bn	^{t}Bu	**5i** (73%)	8:1
10[a]	4-F–C_6H_4	Bn	^{t}Bu	**5j** (67%)	8:1
11[a]	*i*-Pr	Bn	^{t}Bu	**5k** (72%)	8:1
12[b]	*n*-C_5H_{11}	Bn	^{t}Bu	**5l** (57%)	6:1

PMP = 4-methoxyphenyl, PMB = 4-methoxybenzyl.
[a] Reaction carried out in the racemic series.
[b] Reaction carried out by using the enantiomerically pure substrate.

group (entries 4–6). 1,3-Disubstituted pyrrolidinones **5g–l** were consequently obtained with good diastereoselectivities, when using carbamates with *t*-BuO group together with a small *N*-group (entries 7–12). An efficient stereoselective synthesis of 1,3-disubstituted pyrrolidinones would be thus ensured by the suitable tuning of N- and O- protecting groups. The products can be easily deprotected when using carbamates with *N*-PMB group (Section 4).

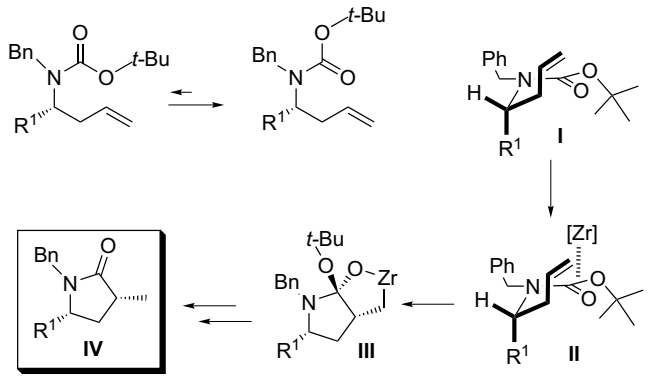
Finally, when using carbamate **4m** with a non-terminal C=C double bond, pyrrolidinone **5m** was obtained in 56% yield as a 3.5:1 mixture of diastereomers (Scheme 5).



4m **5m**

Scheme 5.

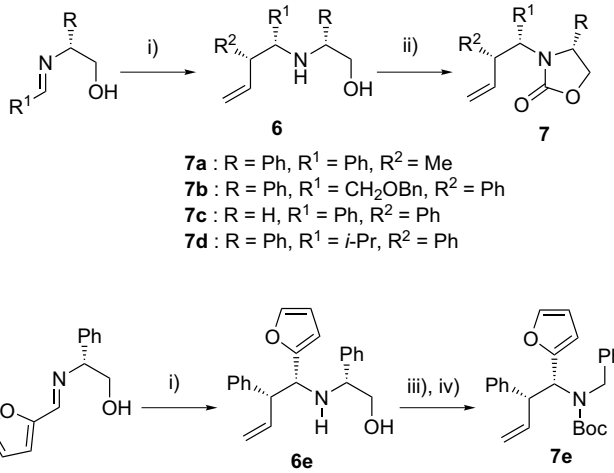
To account for the observed selectivity when using *t*-butyloxy carbamates **4d–l**, we first assumed that the presence of two differently sized substituents (Bn and the homoallyl chain) at the nitrogen atom would preferentially orientate the carbonyl toward the largest homoallyl fragment (Scheme 6). Moreover, it is likely that the R^1 group adopts a pseudo-axial position with respect to the carbamate plan. Therefore, to minimize the steric interactions, and acting as a relay, the flexible protecting group would be located at the opposite side from both the phenyl group and the *t*-butyloxy group as depicted in conformer **I**. Accordingly, the bulky *t*-butyloxy group would cloud selectively one face of the carbonyl moiety, enhancing the approach of the



Scheme 6. Proposed stereochemical rationale.

zirconium complex from the more accessible face of the carbonyl as shown in complex **II**. Thus, the alkene–carbamate coupling reaction affords bicyclic intermediate **III**, precursor of lactam **IV**.

The reaction was next extended to the synthesis of trisubstituted pyrrolidinones. Starting carbamates **7** with an additional substituent at the allylic position (Ph or Me at C_β–N) were synthesized in two steps from the (*R*)-2-phenylglycinol-derived imines (Scheme 7). The amino alcohol precursors were obtained by cerium trichloride-catalyzed allylzinc bromide addition to the corresponding imine in good yield, but with a different level of asymmetric induction.[12] However, they could be isolated in a pure diastereomerical form after separation by column chromatography. Further condensation with triphosgene quantitatively afforded the desired carbamates **7** (Scheme 7). Additionally, opened carbamate **7e** was synthesized from amino alcohol **6e** by $Pb(OAc)_4$ treatment, followed by $NaBH_4$ reduction of the resulting imine and Boc protection.

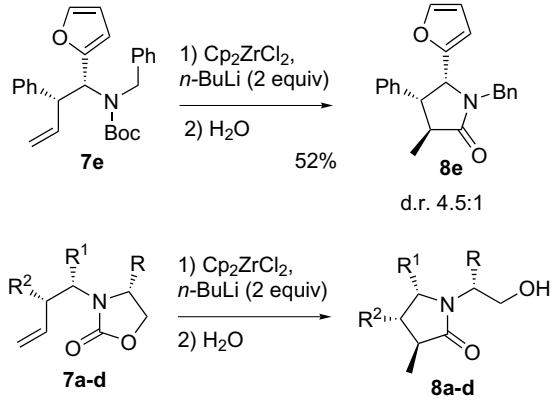


Scheme 7. Synthesis of carbamates **7**. Reagents and conditions: (i) $R^3CH{=}CH{-}CH_2Br$, Zn, $CeCl_3{\cdot}7H_2O$, Zn, THF; (ii) $(Cl_3CO)_2CO$, cat. DMAP, pyridine, CH_2Cl_2; (iii) (a) $Pb(OAc)_4$, CH_2Cl_2, MeOH, (b) $NaBH_4$; (iv) Boc_2O, CH_2Cl_2.

The intramolecular alkene–carbamate coupling reactions were performed as previously described and the results

are shown in Table 3. The trisubstituted pyrrolidinones were obtained from both opened (**7e**) and cyclic (**7a–d**) carbamates in good yields and diastereoselectivities. Aryl, heteroaryl, and alkyl groups can be present on the C_α–N atom of the carbamate leading to pyrrolidinones **8a–e**.

Table 3. Synthesis of trisubstituted pyrrolidinones **8**



Entry	R	R^1	R^2	Compound	dr
1	Ph	Ph	Me	**8a** (65%)	9:1
2	Ph	CH_2OBn	Ph	**8b** (68%)	10:1
3	H	Ph	Ph	**8c** (71%)	12:1
4	Ph	*i*-Pr	Ph	**8d** (53%)	10:1

3. Conclusion

In conclusion, we have described an efficient and straightforward synthesis of optically active di- and trisubstituted pyrrolidinones via a zirconium-mediated alkene–carbamate intramolecular coupling reaction. This reaction is quite general and gives access to diversely substituted pyrrolidines, which are valuable building blocks. Acyclic carbamates have been shown to be more appropriate than the cyclic ones to prepare disubstituted pyrrolidinones in a highly stereoselective way. Cyclic carbamates derived from an amino alcohol can be used for the stereoselective preparation of trisubstituted pyrrolidinones. The easy preparation of starting materials and versatile utility of substituted pyrrolidinones, render this method attractive in organic synthesis.

4. Experimental

4.1. General

All reactions were conducted under an atmosphere of argon using standard Schlenk techniques. Prior to use, tetrahydrofuran and Et_2O were distilled under argon from sodium benzophenone ketyl, NEt_3, CH_3CN, and CH_2Cl_2 were distilled under argon from CaH_2. Reagents (Aldrich) were used as received. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Brucker AC-250. Mass spectra were recorded on a Micromass Q-TOF micro MS spectrometer.

4.2. (*R*)-2-[(*R*)-1-(1-Methyl-1*H*-pyrrol-2-yl)but-3-enylamino]-2-phenylethanol

To a mixture of (*R*)-2-[(1-methyl-1*H*-pyrrol-2-yl)methyleneamino]-2-phenylethanol (1.14 g, 5 mmol), zinc dust (0.82 g, 12.5 mmol), and $CeCl_3{\cdot}7H_2O$ (0.19 g, 0.5 mmol) in THF (20 mL), was added dropwise allylbromide (1.3 mL, 12.5 mmol) at 0 °C. The resulting mixture was stirred for 2 h and quenched with water (20 mL). The layers were separated and the aqueous layer extracted with Et_2O (3×20 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography on silica gel using a mixture of petroleum ether/AcOEt as solvent to give the title compound as a pale yellow oil. $[\alpha]_D^{25} = -44.5$ (*c* 0.9, CH_2Cl_2); ^1H NMR (250 MHz, $CDCl_3$): δ 7.29 (m, 5H), 6.48 (t, 1H, $J = 2.2$ Hz), 6.05 (m, 2H), 5.71 (tdd, 1H, $J = 7.0$, 10.2, 17.1 Hz), 5.04 (dm, 1H, $J = 17.1$ Hz), 5.01 (dm, 1H, $J = 10.2$ Hz), 3.90 (dd, 1H, $J = 4.6$, 7.9 Hz), 3.76 (dd, 1H, $J = 6.0$, 7.3 Hz), 3.66 (d, 1H, $J = 4.6$ Hz), 3.51 (dd, 1H, $J = 8.0$, 10.7 Hz), 3.37 (s, 3H), 2.43–2.63 (m, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 141.0, 135.1, 134.2, 128.6, 127.6, 127.3, 121.9, 117.2, 106.7, 106.3, 66.0, 61.1, 51.5, 39.2, 33.7; IR (film) ν_{max}: 3371, 2926, 2867, 1634, 1053, 701; 3330, 2927, 1491, 1453, 703 cm^{-1}; HRMS-ESI: *m*/*z* $[M+H]^+$ calcd for $C_{17}H_{23}N_2O$: 271.1810; found: 271.1812.

4.3. General procedure for the preparation of carbamates 1a–h (procedure A)

A solution of triphosgene® (148 mg, 1 mmol) in CH_2Cl_2 (2 mL) was added dropwise to a solution of amino alcohol (2 mmol) and pyridine (0.18 mL, 2 mmol) in CH_2Cl_2 (3 mL) at 0 °C. The resulting mixture was stirred for 2 h at rt and diluted with CH_2Cl_2 (10 mL). The organic layer was washed with an aqueous solution of HCl (1 M, 5 mL), dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by column chromatography on silica gel using a mixture of petroleum ether/AcOEt as solvent to give the corresponding carbamate.

4.3.1. (*R*)-4-Phenyl-3-[(*R*)-1-phenylbut-3-enyl]oxazolidin-2-one 1a. Yellow oil; $[\alpha]_D^{25} = -11.0$ (*c* 1.2, CH_2Cl_2); ^1H NMR (250 MHz, $CDCl_3$): δ 7.28 (m, 6H), 7.13 (m, 4H), 5.67 (tdd, 1H, $J = 6.2$, 10.2, 16.8 Hz), 5.01 (t, 1H, $J = 8.0$ Hz), 4.91 (dm, 1H, $J = 10.2$ Hz), 4.86 (dm, 1H, $J = 16.8$ Hz), 4.34 (dd, 1H, $J = 8.0$, 9.0 Hz), 4.23 (dd, 1H, $J = 6.5$, 7.8 Hz), 4.07 (dd, 1H, $J = 6.5$, 8.0 Hz), 2.25 (m, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 174.5, 139.3, 137.5, 134.5, 129.0, 128.9, 128.5, 128.4, 128.1, 127.7, 117.6, 70.2, 58.8, 58.3, 35.7; IR (film): ν_{max} 1725, 14.05, 1235, 1045, 925, 705 cm^{-1}; HRMS-ESI: *m*/*z* $[M+H]^+$ calcd for $C_{19}H_{20}NO_2$: 294.1494; found: 294.1493.

4.3.2. (*R*)-3-[(*R*)-1-(Furan-2-yl)but-3-enyl]-4-phenyloxazolidin-2-one 1b. Red oil; $[\alpha]_D^{25} = -8.5$ (*c* 1, CH_2Cl_2); ^1H NMR (250 MHz, $CDCl_3$): δ 7.36 (dd, 1H, $J = 1.0$, 1.8 Hz), 7.38 (m, 3H), 7.27 (m, 2H), 6.29 (dd, 1H, $J = 2.1$, 3.2 Hz), 6.08 (d, 1H, $J = 3.2$ Hz), 5.55 (tdd, 1H, $J = 6.7$, 10.2, 17.2 Hz), 5.06 (t, 1H, $J = 7.9$ Hz), 5.01 (dm, 1H, $J = 10.2$ Hz), 4.44 (t, 1H, $J = 6.9$ Hz), 4.28 (dd, 1H, $J = 6.7$, 8.7 Hz), 4.05 (dd, 1H, $J = 7.0$, 8.2 Hz), 2.11 (m,

2H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 158.4, 151.3, 142.3, 139.1, 133.7, 128.9, 128.5, 127.5, 117.6, 110.0, 109.0, 70.1, 58.8, 52.7, 35.3; IR (film) v: 2933, 1710, 1640, 1439 cm^{-1}; HRMS-ESI: m/z $[M+Na]^+$ calcd for $C_{17}H_{17}NO_3$: 306.1116; found: 306.1111.

4.3.3. (*R*)-3-[(*R*)-1-(1-Methyl-1*H*-pyrrol-2-yl)but-3-enyl]-4-phenyloxazolidin-2-one 1c. Yellow oil; $[\alpha]_D^{25} = -15.5$ (c 1, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.35 (m, 3H), 7.25 (m, 2H), 6.68 (dd, 1H, $J = 1.7$, 2.8 Hz), 6.09 (dd, 1H, $J = 2.8$, 3.5 Hz), 5.88 (dd, 1H, $J = 1.7$, 3.5 Hz), 5.70 (dddd, 1H, $J = 6.0$, 7.0, 10.5, 17.0 Hz), 4.99 (dm, 1H, $J = 17.0$ Hz), 4.88 (dm, 1H, $J = 10.5$ Hz), 4.48 (t, 1H, $J = 11.3$ Hz), 4.17 (dd, 1H, $J = 2.7$, 6.5 Hz), 4.12 (dd, 1H, $J = 2.2$, 6.7 Hz), 3.60 (s, 3H), 2.22–2.02 (m, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 181.0, 158.2, 139.9, 134.5, 129.0, 128.7, 127.8, 123.2, 117.5, 109.6, 106.7, 70.4, 57.7, 50.8, 36.9, 33.9; IR (film): ν_{max} 1750, 1404, 1218, 1423, 701 cm^{-1}; HRMS-ESI: m/z $[M+Na]^+$ calcd for $C_{18}H_{20}N_2O_2$: 319.1422; found: 319.1425.

4.3.4. (*R*)-3-[(*R*)-1-(2-Methoxyphenyl)but-3-enyl]-4-phenyloxazolidin-2-one 1d. Yellow oil; $[\alpha]_D^{25} = -19$ (c 0.8, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.32 (m, 4H), 7.08 (m, 2H), 6.96 (t, 1H, $J = 7.0$ Hz), 6.90 (d, 2H, $J = 8.5$ Hz), 5.78 (tdd, 1H, $J = 6.5$, 10.0, 17.2 Hz), 5.33 (dd, 1H, $J = 7.5$, 9.0 Hz), 5.02 (dm, 1H, $J = 10.0$ Hz), 4.96 (dm, 1H, $J = 17.0$ Hz), 4.40 (t, 1H, $J = 8.2$ Hz), 4.03 (dt, 1H, $J = 7.6$ Hz), 3.80 (s, 3H), 2.32 (m, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 158.7, 157.6, 139.6, 135.0, 129.3, 128.8, 128.7, 128.6, 127.7, 125.1, 119.9, 117.4, 110.2, 70.0, 59.1, 55.4, 52.5, 36.2; IR (film): ν_{max} 1755, 1490, 1450 cm^{-1}; HRMS-ESI: m/z $[M+Na]^+$ calcd for $C_{20}H_{22}NO_3$: 324.1600; found: 324.1597.

4.3.5. (*R*)-3-[(*R*)-2-Methylhex-5-en-3-yl]-4-phenyloxazolidin-2-one 1e. Yellow oil; $[\alpha]_D^{25} = -14$ (c 0.8, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.38 (m, 5H), 5.76 (tdd, 1H, $J = 6.0$, 10.2, 17.0 Hz), 5.04 (dm, 1H, $J = 10.2$ Hz), 4.96 (dm, 1H, $J = 17.2$ Hz), 4.75 (dd, 1H, $J = 7.0$, 9.0 Hz), 4.58 (t, 1H, $J = 8.7$ Hz), 4.23 (dd, 1H, $J = 6.7$, 8.7 Hz), 3.07 (dt, 1H, $J = 4.0$, 10.2 Hz), 2.12 (m, 2H), 0.88 (d, 3H, $J = 6.7$ Hz), 0.81 (d, 3H, $J = 6.7$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 151.9, 138.7, 135.6, 129.1, 128.9, 128.2, 117.4, 69.8, 61.3, 60.7, 34.7, 29.8, 20.6, 20.4; IR (film): ν_{max} 1745, 1410, 1220 cm^{-1}; HRMS-ESI: m/z $[M+Na]^+$ calcd for $C_{16}H_{21}NO_2Na$: 282.1470; found: 282.1471.

4.3.6. 3-(1-Phenylbut-3-enyl)oxazolidin-2-one 1f. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.35 (m, 5H), 5.82 (dddd, 1H, $J = 6.0$, 7.5, 10.2, 17.3 Hz), 5.24–5.08 (m, 2H), 4.34–4.16 (m, 2H), 3.50 (ddd, 1H, $J = 6.5$, 8.2, 9.0 Hz), 3.20 (ddd, 1H, $J = 7.5$, 8.2, 9.0 Hz), 2.85–2.64 (m, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 158.2, 138.1, 134.1, 128.7, 128.0, 127.4, 117.8, 61.9, 55.6, 40.0, 34.7; IR (film): ν_{max} 2918, 1733, 1423, 1252, 703 cm^{-1}; HRMS-ESI: m/z $[M+Na]^+$ calcd for $C_{13}H_{15}NO_2Na$: 240.1000; found: 240.0998.

4.3.7. 3-[1-(2-Methoxyphenyl)but-3-enyl]oxazolidin-2-one 1g. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.30 (m, 2H), 6.92 (m, 2H), 5.82 (m, 1H), 5.35 (dd, 1H, $J = 6.5$, 9.2 Hz), 5.18 (dm, 1H, $J = 17.5$ Hz), 5.08 (dm, 1H, $J = 10.7$ Hz), 4.15–4.30 (m, 2H), 3.84 (s, 3H), 3.54 (td, 1H, $J = 6.1$, 8.4 Hz), 3.22 (td, 1H, $J = 6.9$, 8.4 Hz), 2.78 (m, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 157.8, 157.5, 134.7, 129.2, 128.0, 126.3, 120.2, 117.5, 110.8, 61.8, 55.4, 51.1, 41.5, 34.9; IR (film): ν_{max} 2920, 1745, 1492, 1421, 1248 cm^{-1}; HRMS-ESI: m/z $[M+Na]^+$ calcd for $C_{14}H_{17}NO_2Na$: 270.1006; found: 270.1008.

4.3.8. 3-[(*E*)-1-Phenylhexa-1,5-dien-3-yl]oxazolidin-2-one 1h. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.40–7.25 (m, 5H), 6.58 (dd, 1H, $J = 1.2$, 16.0 Hz), 6.16 (dd, 1H, $J = 6.5$, 16.0 Hz), 5.82 (tdd, 1H, $J = 6.0$, 10.0, 17.0 Hz), 5.18 (dm, 1H, $J = 17.0$ Hz), 5.13 (dm, 1H, $J = 10.0$ Hz), 4.65 (td, 1H, $J = 6.5$, 8.8 Hz), 4.33 (t app, 1H, $J = 8.0$ Hz), 3.53 (t app, 1H, $J = 7.8$ Hz), 2.55 (ddm, 1H, $J = 6.5$, 14.2 Hz), 2.46 (ddm, 1H, $J = 8.7$, 14.2 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 133.9, 132.7, 128.6, 128.0, 126.4, 126.0, 117.9, 62.0, 54.1, 40.4, 36.2, 2C are missing; IR (film): ν_{max} 2917, 1742, 1425, 1254 cm^{-1}; HRMS-ESI: m/z $[M+Na]^+$ calcd for $C_{15}H_{17}NO_2Na$: 266.1157; found: 266.1154.

4.4. General procedure for the preparation of pyrrolidinones 2a–h (procedure B)

To a solution of Cp_2ZrCl_2 (292 mg, 1 mmol) in THF (5 mL) was added dropwise a solution of n-BuLi (1.6 in hexane, 1.25 mL, 2 mmol) at −78 °C under Ar. The resulting solution was stirred at −78 °C for 30 min, then a solution of carbamates **1**, **4**, or **7** (1 mmol) in THF (2 mL) was added dropwise at this temperature. The reaction was slowly warmed to room temperature, and then stirred for 6 h. The reaction was quenched by adding an aqueous solution of HCl (1 M, 2 mL). The aqueous layer was extracted with AcOEt (3 × 5 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by column chromatography on silica gel using a mixture of petroleum ether/AcOEt as solvent to give the corresponding pyrrolidinone.

4.4.1. (3*S*,5*R*)-1-[(*R*)-2-Hydroxy-1-phenylethyl]-3-methyl-5-phenylpyrrolidin-2-one 2a. Major diastereomer: White solid; $[\alpha]_D^{25} = -22.5$ (c 1.1, CH_2Cl_2); mp 106 °C ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.28 (m, 6H), 7.10 (m, 4H), 5.22 (dd, 1H, $J = 6.0$, 8.3 Hz), 4.28 (dd, 1H, $J = 3.1$, 8.5 Hz), 3.86–3.62 (m, 2H), 2.89 (m, 1H), 2.75 (br m, 1H), 2.15–1.86 (m, 2H), 1.24 (d, 3H, $J = 7.1$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 179.6, 142.2, 136.3, 128.7, 128.5, 128.3, 128.0 (2C), 126.4, 63.1, 60.3, 59.5, 38.1, 35.4, 16.3; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{19}H_{22}NO_2$: 296.1651; found: 296.1644; Anal. Calcd for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.38; H, 7.26; N, 4.63.

4.4.2. 5-(Furan-2-yl)-1-[(*R*)-2-hydroxy-1-phenylethyl]-3-methylpyrrolidin-2-one 2b. Red oil; major diastereomer (3*S*,5*R*): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.28 (m, 4H), 7.15 (m, 2H), 6.25 (dd, 1H, $J = 1.8$, 3.2 Hz), 6.07 (d, 1H, $J = 0.7$, 3.2 Hz), 5.17 (dd, 1H, $J = 6.5$, 7.5 Hz), 4.34 (dd, 1H, $J = 2.8$, 8.7 Hz), 3.77 (m, 2H), 2.99 (qdd, 1H, $J = 7.1$, 8.5, 9.5 Hz), 2.28 (ddd, 1H, $J = 2.8$, 8.2,

12.6 Hz), 1.89 (ddd, 1H, $J = 8.7$, 9.5, 12.6 Hz), 1.26 (d, 3H, $J = 7.1$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 178.9, 153.7, 142.4, 136.2, 128.6, 128.5, 128.0, 127.8, 110.4, 107.6, 62.6, 59.2, 53.1, 35.9, 34.7, 16.1; IR (film): ν_{max} 3402, 2971, 2933, 2876, 1677, 1454, 1418, 1251, 1062, 1012, 749, 699 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{17}H_{20}NO_3$: 286.1443; found: 286.1448.

4.4.3. 1-[(*R*)-2-Hydroxy-1-phenylethyl]-3-methyl-5-(1-methyl-1*H*-pyrrol-2-yl)pyrrolidin-2-one 2c. Yellow oil; major diastereomer (3*S*,5*R*): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.30 (m, 3H), 7.11 (m, 2H), 6.49 (dd, 1H, $J = 2.0$, 2.7 Hz), 6.10 (dd, 1H, $J = 2.0$, 3.7 Hz), 6.05 (dd, 1H, $J = 2.7$, 3.5 Hz), 5.20 (dd, 1H, $J = 5.2$, 8.0 Hz), 4.39 (dd, 1H, $J = 3.2$, 8.5 Hz), 3.98 (ddd, 1H, $J = 6.2$, 8.0, 11.5 Hz), 3.85 (td, 1H, $J = 5.0$, 11.5 Hz), 3.09 (s, 3H), 2.90 (qt, 1H, $J = 7.0$, 8.5 Hz), 2.73 (br t, 1H, $J = 5.7$ Hz), 2.14 (ddd, 1H, $J = 3.0$, 8.2, 12.5 Hz), 1.90 (td, 1H, $J = 8.7$, 12.5 Hz), 1.25 (d, 3H, $J = 7.0$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 179.1, 136.5, 131.7, 128.6, 128.3, 128.0, 122.9, 107.3, 63.2, 59.0, 52.2, 36.4, 35.2, 33.6, 16.1; IR (film): ν_{max} 3411, 2967, 1674, 753, 702 cm^{-1}; HRMS-ESI: m/z $[M+Na]^+$ calcd for $C_{18}H_{22}N_2O_2$: 321.1579; found: 321.1573.

4.4.4. (3*S*,5*R*)-1-[(*R*)-2-Hydroxy-1-phenylethyl]-5-(2-methoxyphenyl)-3-methylpyrrolidin-2-one 2d. Major diastereomer: Yellow oil; $[\alpha]_D^{25} = +46$ (c 1.2, CH_2Cl_2); ^{1}H NMR: δ 7.23 (m, 4H), 7.08 (m, 3H), 6.86 (t, 1H, $J = 7.4$ Hz), 6.77 (d, 1H, $J = 8.0$ Hz), 5.09 (dd, 1H, $J = 5.2$, 7.7 Hz), 5.64 (d, 1H, $J = 7.0$ Hz), 3.82 (m, 2H), 3.70 (s, 3H), 2.98–2.80 (m, 2H), 2.12 (dd, 1H, $J = 10.0$, 12.7 Hz), 1.95 (dt, 1H, $J = 9.2$, 12.7 Hz), 1.25 (d, 3H, $J = 7.0$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 180.1, 156.6, 136.6, 129.6, 129.1, 128.6, 128.3, 127.7, 120.4, 110.7, 63.6, 60.1, 55.1, 36.2, 35.8, 16.7, 2C are missing; IR (film): ν_{max} 3403, 2963, 2932, 1668, 1492, 1464, 1244, 1026, 755 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{20}H_{24}NO_3$: 326.1756; found: 326.1753.

4.4.5. (3*S*,5*R*)-1-[(*R*)-2-Hydroxy-1-phenylethyl]-5-isopropyl-3-methylpyrrolidin-2-one 2e. Major diastereomer: Yellow oil; $[\alpha]_D^{25} = +24.5$ (c 0.3, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.34 (m, 5H), 4.69 (dd, 1H, $J = 4.4$, 7.6 Hz), 4.23 (td, 1H, $J = 7.9$, 11.2 Hz), 4.08 (td, 1H, $J = 3.7$, 11.2 Hz), 3.87 (dd, 1H, $J = 4.3$, 7.7 Hz), 3.33 (dm, 1H, $J = 9.2$ Hz), 2.62 (m, 1H), 2.06 (dd, 1H, $J = 10.5$, 11.4 Hz), 1.82 (m, 1H), 1.60 (td, 1H, $J = 9.5$, 12.2 Hz), 1.23 (d, 3H, $J = 7.1$ Hz), 0.77 (d, 3H, $J = 6.9$ Hz), 0.61 (d, 3H, $J = 6.7$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 179.7, 137.6, 128.6, 128.0, 127.7, 64.9, 64.6, 62.5, 36.9, 30.3, 27.8, 19.2, 17.3, 14.5; IR (film): ν_{max} 3395, 2963, 1661, 1451, 1065, 755, 701 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{16}H_{24}NO_2$: 262.1807; found: 262.1804.

4.4.6. 1-(2-Hydroxyethyl)-3-methyl-5-phenylpyrrolidin-2-one 2f. Yellow oil; major isomer: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.27 (m, 3H), 7.10 (dd, 2H, $J = 2.0$, 8.1 Hz), 4.65 (t, 1H, $J = 6.1$ Hz), 3.58 (m, 4H), 2.88 (m, 1H), 2.65 (m, 1H), 2.09 (m, 2H), 1.18 (d, 3H, $J = 7.2$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 161.5, 140.8, 128.9, 127.9, 127.1, 126.2, 61.6, 60.7, 44.9, 37.3, 35.2, 16.3; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{13}H_{18}NO_2$: 220.1338; found: 220.1342.

4.4.7. 1-(2-Hydroxyethyl)-5-(2-methoxyphenyl)-3-methylpyrrolidin-2-one 2g. Yellow oil; major isomer: ^{1}H NMR: δ 7.28 (dt, 1H, $J = 1.9$, 7.5 Hz), 6.97 (m, 3H), 5.04 (dd, 1H, $J = 4.8$, 6.7 Hz), 3.72–3.58 (m, 3H), 3.01 (m, 2H), 2.66 (hex, 1H, $J = 7.8$ Hz), 2.13 (m, 2H), 1.23 (d, 3H, $J = 7.1$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 180.2, 156.9, 128.8, 128.4, 126.1, 120.5, 110.7, 61.1, 56.4, 55.3, 45.6, 36.0, 35.1, 16.2; IR (film): ν_{max} 3403, 2965, 2933, 1668, 1491, 1463, 1243, 755 cm^{-1}; MS-ESI: m/z $[M+H]^+$: 249.

4.4.8. (*E*)-1-(2-Hydroxyethyl)-3-methyl-5-styrylpyrrolidin-2-one 2h. Yellow oil; major isomer: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.40–7.26 (m, 5H), 6.54 (d, 1H, $J = 15.8$ Hz), 6.04 (dd, 1H, $J = 8.6$, 15.8 Hz), 4.25 (dt, 1H, $J = 3.8$, 8.2 Hz), 3.73 (t, 1H, $J = 5.1$ Hz), 3.60 (m, 1H), 3.22 (td, 1H, $J = 4.0$, 14.8 Hz), 2.67 (hex, 1H, $J = 7.6$ Hz), 2.13 (ddd, 1H, $J = 3.9$, 8.5, 12.8 Hz), 2.00 (dt, 1H, $J = 4.5$, 8.0 Hz), 1.24 (d, 3H, $J = 7.2$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 179.2, 135.7, 134.2, 132.8, 128.6, 128.1, 126.5, 61.2, 60.4, 44.7, 35.4, 34.8, 16.3; IR (film): ν_{max} 3389, 2967, 2932, 1668, 1456, 753 cm^{-1}; MS-ESI: m/z $[M+H]^+$: 245.

4.5. (3*S*,5*R*)-3-Methyl-5-phenylpyrrolidin-2-one *trans*-3

A solution of **2a** (210 mg, 0.71 mmol) and thionyl chloride (165 mg, 1.4 mmol) in CH_2Cl_2 (3 mL) was stirred at rt for 2 h. The solvent and the excess of thionyl chloride was removed under vacuum. The residue was dissolved in CH_3CN (3 mL) and DBU (0.34 mL, 2.3 mmol) was added and the resulting mixture stirred overnight. The solvent was removed under vacuum and the residue dissolved in CH_2Cl_2 (2 mL). A solution of HCl (5 M, 0.8 mL) was added and the resulting mixture stirred vigorously for 30 min at rt. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3×3 mL). The organic layers were combined, dried over Na_2SO_4, and concentrated to give the lactam **3**-*trans*, as white needles, after column chromatography on silica gel using a mixture of petroleum ether/AcOEt as solvent. Mp 139 °C, $[\alpha]_D^{25} = +39$ (c 0.5, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.30 (m, 5H), 6.95, (br s, 1H), 4.73 (dd, 1H, $J = 5.9$, 6.3 Hz), 2.61 (hex, 1H, $J = 7.2$ Hz), 2.21 (m, 2H), 1.23 (d, 3H, $J = 7.2$ Hz).

4.6. General procedure for the preparation of carbamates 4a–l

To a solution of amine and DMAP (12 mg, 0.1 mmol) in CH_2Cl_2 (3 mL) was added dropwise a solution of $(Boc)_2O$ (275 mg, 1.25 mmol) in CH_2Cl_2 (2 mL) at rt. The reaction mixture was then stirred for 4 h at rt and quenched by adding water (2 mL). The aqueous layer was extracted with dichloromethane (3×5 mL), the organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under vacuum. The residue was purified by column chromatography on silica gel using a mixture of petroleum ether/AcOEt as eluant to give the corresponding carbamate **4**.

4.6.1. *tert*-Butyl 4-methoxyphenyl(1-phenylbut-3-enyl)carbamate 4a. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.27 (m, 3H), 7.20 (m, 2H), 6.70 (m, 4H), 5.88 (dddd, $J = 6.1$, 6.7, 10.2, 17.1 Hz, 1H), 5.71 (dd, $J = 6.9$, 9.0 Hz, 1H), 5.19 (dm, $J = 17.1$ Hz, 1H), 5.14 (dm, $J = 10.2$ Hz, 1H), 3.75 (s, 3H), 2.68 (m, 2H), 1.38 (s, 9H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 27.3, 35.0, 55.2, 60.8, 84.3, 113.6, 117.9, 128.0, 128.2, 128.5, 130.4, 134.3, 138.4, 147.8, 149.8, 159.1; IR (film): ν_{max} 2980, 1775, 1733, 1512, 1219, 1148 cm^{-1}.

4.6.2. *tert*-Butyl 1-phenylbut-3-enyl(propyl)carbamate 4d. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.30 (m, 5H), 5.82 (tdd, 1H, $J = 6.7$, 10.2, 17.1 Hz), 5.71 (br m, 1H), 5.19 (dd, 1H, $J = 1.4$, 17.1 Hz), 5.06 (dm, 1H, $J = 10.2$ Hz), 2.88 (m, 2H), 2.72 (m, 2H), 1.38 (s, 9H), 1.20 (br m, 2H), 0.68 (t, 3H, $J = 7.4$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 155.9, 140.5, 135.1, 128.1, 127.7, 127.1, 117.0, 79.2, 35.5, 28.4, 22.6, 11.4, 1C is missing; MS-ESI: m/z $[M+H]^+$: 289.

4.6.3. *tert*-Butyl benzyl(1-phenylbut-3-enyl)carbamate 4e. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.38–7.02 (m, 5H), 5.72 (m, 1H), 5.49 (br m, 1H), 5.04–4.97 (m, 2H), 4.31 (br m, 1H), 4.07 (d, 1H, $J = 14.9$ Hz), 3.76 (s, 3H), 2.65 (dd, 2H, $J = 7.0$, 7.5 Hz), 1.39 (br s, 9H), ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 156.1, 140.0, 139.6, 135.1, 128.3, 128.0, 127.4, 126.5, 117.1, 80.0, 36.0, 28.5, 4C are missing; MS-ESI: m/z $[M+H]^+$: 338.

4.6.4. *tert*-Butyl 4-methoxybenzyl(1-phenylbut-3-enyl)carbamate 4f. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.28 (m, 5H), 6.98 (br s, 2H), 6.74 (d, $J = 8.3$ Hz, 2H), 5.71 (tdd, $J = 6.7$, 10.3, 17.2 Hz, 1H), 5.36 (br m, 1H), 4.99 (br d, $J = 17.2$ Hz, 1H), 4.98 (br d, $J = 10.3$ Hz, 1H), 4.28 (br s, 1H), 4.00 (d, $J = 15.5$ Hz, 1H), 3.76 (s, 3H), 2.64 (t, $J = 7.0$ Hz, 2H), 1.41 (br s, 9H); ^{13}C NMR: δ 158.3, 156.1, 140.1, 135.2, 131.7, 128.8, 128.2, 128.1, 127.3, 117.1, 113.4, 79.9, 58.7, 55.2, 46.9, 35.9, 28.4; IR (film) ν: 2977, 2932, 1684, 1513, 1247, 1163 cm^{-1}; MS-ESI: m/z $[M+H]^+$: 367.

4.6.5. *tert*-Butyl benzyl(1-(4-methoxyphenyl)but-3-enyl)carbamate 4g. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.20 (m, 5H), 7.06 (br m, 2H), 6.82 (d, 2H, $J = 8.5$ Hz), 5.84–5.60 (m, 1H), 5.45 (br m, 1H), 4.99 (br d, 1H, $J = 18.2$ Hz), 4.97 (br d, 1H, $J = 10.1$ Hz), 4.30 (br m, 1H), 4.05 (d, 1H, $J = 15.8$ Hz), 3.75 (s, 3H), 2.61 (dd, 2H, $J = 6.7$, 7.4 Hz), 1.39 (br s, 9H); ^{13}C NMR: δ 158.7, 156.0, 139.6, 135.1, 131.8, 129.2, 127.8, 127.1, 126.4, 116.9, 113.5, 79.7, 57.7, 55.0, 47.0, 36.0, 28.2; IR (film): ν_{max} 2976, 2932, 1685, 1513, 1250, 1161 cm^{-1}; MS-ESI: m/z $[M+H]^+$: 367.

4.6.6. *tert*-Butyl 4-methoxybenzyl[1-(2-methoxyphenyl)but-3-enyl]carbamate 4h. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.30–6.65 (br m, 8H), 5.71 (br m, 1H), 5.49 (br s, 1H), 4.91–5.04 (br m, 2H), 4.13 (br s, 2H), 3.75 (br s, 3H), 3.73 (br s, 3H), 2.60 (br s, 2H), 1.47 (br s, 9H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 158.1, 157.9, 135.6, 132.1, 128.7, 128.4 (br signal), 127.5, 119.8, 116.7, 113.1, 110.2, 55.2, 55.1, 46.8, 28.4; MS-ESI: m/z $[M+H]^+$: 397.

4.6.7. *tert*-Butyl benzyl[1-(furan-2-yl)but-3-enyl]carbamate 4i. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.00–7.26 (br m, 6H), 6.26–6.04 (br m, 2H), 5.81–5.50 (br m, 1.5H), 5.20–4.92 (br m, 2.5H), 4.31 (br m, 1H), 4.17 (d, $J = 15.8$ Hz, 1H), 2.57 (br s, 2H), 1.47–1.33 (s, 9H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 155.6, 153.1, 141.6, 139.4, 134.1, 127.7, 126.5, 126.2, 117.3, 109.8, 79.8, 52.4, 46.9, 35.5, 28.1; IR (film): ν_{max} 2977, 2931, 1699, 1454, 1164, 735 cm^{-1}; MS-ESI: m/z $[M+H]^+$: 327.

4.6.8. *tert*-Butyl benzyl[1-(4-fluorophenyl)but-3-enyl]carbamate 4j. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.10 (m, 5H), 6.96 (br m, 2H), 6.83 (t, 2H, $J = 7.7$ Hz), 5.60 (br m, 1H), 5.28 (br m, 1H), 4.92 (br m, 2H), 4.20 (br m, 1H), 4.02 (d, 1H, $J = 15.7$ Hz), 2.54 (m, 2H), 1.30 (s, 9H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 161.9 (d, $J = 245$ Hz), 155.9, 137.5 (d, $J = 225$ Hz), 134.8, 129.7, 127.9, 127.2, 126.6, 117.3, 114.9 (d, $J = 21$ Hz), 80.0, 57.9, 47.4, 35.9, 28.2; IR (film): ν_{max} 2977, 2930, 1685, 1511, 1226, 1157 cm^{-1};^{19}F NMR: δ −115.3 (br m); MS-ESI: m/z $[M+H]^+$: 355.

4.6.9. *tert*-Butyl benzyl(2-methylhex-5-en-3-yl)carbamate 4k. Yellow oil; obtained as a mixture of two rotamers: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.26 (m, 5H), 5.66 (m, 0.5H), 5.51 (m, 0.5H), 4.99–4.85 (m, 2H), 4.35 (s, 1H), 4.24 (s, 1H), 3.77 (br m, 0.5H), 2.34 (br m, 0.5H), 1.84 (br m, 1H), 1.50 (s, 4.5H), 1.36 (s, 4.5H), 0.90 (br m, 3H), 0.81 (d, $J = 6.2$ Hz, 1.5H), 0.71 (d, $J = 5.1$ Hz, 1.5H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 156.5, 156.0, 139.6, 139.1, 135.9, 135.8, 128. 4, 127.9, 127.8, 127.4, 126.6, 126.4, 116.1 (2C), 79.3, 79.1, 64.2, 62.8, 48.5, 48.4, 35.5, 34.8, 31.4, 30.9, 28.3, 28.1, 20.6 (2C), 20.2, 20.0; IR (film): ν_{max} 2975, 2873, 1684, 1365, 1166, 701 cm^{-1}; MS-ESI: m/z $[M+H]^+$: 301.

4.6.10. *tert*-Butyl benzyl(non-1-en-4-yl)carbamate 4l. Yellow oil; $[\alpha]_D^{25} = -11.9$ (c 1, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.26 (m, 5H), 5.67 (br m, 1H), 4.95 (br m, 2H), 4.37 (br s, 0.9H), 4.26 (br s, 1.1H), 4.14 (br t, 0.55H, $J = 6.5$ Hz), 3.75 (br s, 0.45H), 2.15 (m, 2H), 1.52–1.08 (br m, 17H), 0.75 (t, $J = 6.6$ Hz, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 154.0, 136.4, 136.2, 128.5, 127.5, 127.0, 117.0, 79.8, 56.6, 47.7, 47.6, 39.0, 38.6, 33.7, 33.1, 32.1, 29.0, 28.8, 26.7, 23.0, 14.4; IR (film): ν_{max} 2983, 2869, 1686, 1361, 1162, 709 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{21}H_{33}NO_2$: 331.2511; found: 331.2515.

4.7. (*E*)-*tert*-Butyl 1,4-diphenylbut-3-enyl(4-methoxybenzyl)carbamate 4m

A mixture of *N*-(4-methoxybenzyl)-1-phenylbut-3-en-1-amine (2.67 g, 10 mmol), iodobenzene (2.45 g, 12 mmol), and anhydrous $NaHCO_3$ (2.52 g, 30 mmol) and $Pd(OAc)_2$ (224 mg, 1 mmol) in acetonitrile (20 mL) was heated to reflux overnight. Water (10 mL) was added and the aqueous layer extracted with AcOEt (2 × 10 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated under vacuum. Boc_2O (2.6 g, 10 mmol) and DMAP (50 mg, 0.4 mmol) and CH_2Cl_2 (20 mL) were added to the crude mixture, and the reaction was stirred for 4 h at rt. This solution was washed with an aqueous solution of HCl (1 M, 5 mL). The aqueous layer was extracted with

AcOEt (2×5 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by column chromatography on silica gel using a mixture of petroleum ether/AcOEt as solvent to give **4m** as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.24 (m, 10H), 7.00 (br m, 2H), 6.73 (d, 2H, $J = 8.3$ Hz), 6.25 (d, 1H, $J = 16.0$ Hz), 6.04 (br m, 1H), 5.43 (br m, 1H), 4.31 (br m, 1H), 4.06 (d, 1H, $J = 15.4$ Hz), 3.75 (s, 3H), 2.64–2.90 (m, 2H), 1.40 (s, 9H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 158.3, 156.1, 140.3, 137.4, 132.0, 131.6, 128.5, 128.3 (2C), 127.9, 127.0, 126.9, 126.0, 113.4, 55.1, 47.3, 35.4, 28.3.

4.8. Preparation of pyrrolidinone 5

4.8.1. 1-(4-Methoxyphenyl)-3-methyl-5-phenylpyrrolidin-2-one 5a. Obtained as a 1.5:1 mixture of diastereomers according to procedure B. Minor diastereomer: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.40 (d, 2H, $J = 9.0$ Hz), 7.32–7.19 (m, 5H), 6.78 (d, 2H, $J = 9.0$ Hz), 5.12 (dd, 1H, $J = 4.0$, 6.8 Hz), 3.73 (s, 3H), 2.84 (qt, 1H, $J = 7.1$, 9.1 Hz), 2.25 (dd, 1H, $J = 3.9$, 9.1 Hz), 2.23 (d, 1H, $J = 9.1$ Hz), 1.30 (d, 3H, $J = 7.1$ Hz); ^{13}C NMR: δ 177.0, 156.5, 141.3, 131.8, 128.9, 127.6, 125.8, 123.0, 113.9, 61.9, 55.3, 37.8, 35.7, 15.9. Major diastereomer: ^{1}H NMR: δ 7.24–7.19 (m, 7H), 6.74 (d, 2H, $J = 9.1$ Hz), 5.08 (dd, 1H, $J = 6.9$, 8.9 Hz), 3.69 (s, 3H), 2.85–2.64 (m, 2H), 1.64 (ddd, 1H, $J = 2.7$, 8.5, 17.4 Hz), 1.36 (d, 3H, $J = 7.1$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 177.2, 156.7, 141.3, 131.0, 128.7, 127.6, 126.6, 124.7, 113.8, 62.2, 55.2, 38.9, 37.5, 16.6; IR (film): ν_{max} 1694, 1512, 1248 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{18}H_{20}NO_2$: 282.1494; found: 282.1500.

4.8.2. 1-Benzyl-3-methyl-5-phenylpyrrolidin-2-one 5b. Obtained according to procedure B using **4e** as starting material. Yellow oil. Major isomer (3*RS*,5*RS*)-: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.36 (d, 2H, $J = 7.3$ Hz), 7.24 (m, 4H), 7.14 (d, 2H, $J = 7.7$ Hz), 7.01 (dd, 2H, $J = 2.9$, 6.4 Hz), 5.08 (d, 1H, $J = 14.5$ Hz), 4.27 (dd, 1H, $J = 8.3$, 7.2 Hz), 3.48 (d, 1H, $J = 14.5$ Hz), 2.67–2.49 (m, 2H), 1.53 (td, 1H, $J = 8.4$, 5.7 Hz), 1.33 (d, 3H, $J = 6.5$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 178.3, 140.9, 136.8, 129.3, 129.1, 128.9, 128.5, 127.8, 127.7, 126.9, 60.3, 44.9, 38.7, 37.3, 35.7, 16.9; IR (film): ν_{max} 3466, 2930, 1691, 1455, 1241, 700 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{18}H_{20}NO$: 266.1545; found: 266.1542.

4.8.3. (3*RS*,5*RS*)-3-Methyl-1-propyl-5-phenylpyrrolidin-2-one 5d. Obtained according to procedure B. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.22–7.41 (m, 5H), 4.52 (dd, 1H, $J = 8.9$, 6.6 Hz), 3.59 (dt, 1H) , $J = 8.4$, 6.0 Hz, 2.53 (m, 3H), 1.32–1.53 (m, 3H), 1.28 (d, 3H, $J = 6.8$ Hz), 0.78 (t, 3H, $J = 7.3$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 178.0, 141.0, 129.0, 128.2, 127.2, 60.7, 42.3, 38.7, 36.9, 20.1, 16.5, 11.4; IR (film): ν_{max} 2965, 2932, 2874, 1690, 1456, 1418, 702 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{14}H_{20}NO$: 218.1545; found: 218.1546.

4.8.4. 1-(4-Methoxybenzyl)-3-methyl-5-phenylpyrrolidin-2-one 5f. Obtained according to procedure B. Yellow oil; Major isomer (3*RS*,5*RS*): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.35 (m, 4H), 6.95 (d, 2H, $J = 8.8$ Hz), 6.78 (d, 2H, $J = 8.8$ Hz), 5.05 (d, 1H, $J = 14.4$ Hz), 4.25 (dd, 1H, $J = 8.5$, 7.1 Hz), 3.78 (s, 3H), 3.44 (d, 1H, $J = 14.4$ Hz), 2.54 (m, 2H), 1.52 (dt, 1H, $J = 12.2$, 9.7 Hz), 1.31 (t, 3H, $J = 6.8$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 177.7, 159.5, 136.5, 132.2, 128.7, 128.6, 128.4, 127.4, 114.2, 59.3, 55.3, 44.3, 38.4, 36.9, 16.4; IR (film): ν_{max} 2964, 2932, 1688, 1513, 1248, 1176, 1033 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{19}H_{22}NO_2$: 296.1651; found: 296.1646.

4.8.5. (3*RS*,5*RS*)-1-Benzyl-5-(4-methoxyphenyl)-3-methylpyrrolidin-2-one 5g. Obtained according to procedure B. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.21 (m, 3H), 7.04–6.97 (m, 4H), 6.87 (dd, 2H, $J = 8.6$, 2.0 Hz), 5.01 (d, 1H, $J = 14.5$ Hz), 4.20 (t, 1H, $J = 6.9$ Hz), 3.79 (s, 3H), 3.44 (d, 1H, $J = 14.5$ Hz), 2.57–2.46 (m, 2H), 1.49 (ddt, 1H, $J = 8.5$, 8.5, 6.1, 2.1 Hz), 1.30 (d, 3H, $J = 6.7$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 177.7, 159.5, 136.6, 132.2, 128.8, 128.5, 127.4, 114.3, 59.4, 55.3, 44.4, 38.4, 37.0, 16.5; IR (film): ν_{max} 3458, 2932, 2873, 1687, 1513, 1248, 1033 cm^{-1}.

4.8.6. 1-(4-Methoxybenzyl)-5-(2-methoxyphenyl)-3-methylpyrrolidin-2-one 5h. Obtained according to procedure B. Yellow oil; (3*RS*,5*RS*)-isomer: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.28 (m, 1H), 7.12–6.85 (m, 5H), 6.76 (d, 2H, $J = 8.7$ Hz), 4.98 (d, 1H, $J = 14.4$ Hz), 4.73 (t, 1H, $J = 7.0$ Hz), 3.77 (s, 3H), 3.72 (s, 3H), 3.48 (d, 1H, $J = 14.4$ Hz), 2.56 (m, 2H), 1.54 (m, 1H), 1.25 (d, 3H, $J = 6.6$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 177.9, 158.8, 157.3, 130.0, 128.8, 128.5, 120.8, 113.6, 110.9, 55.25, 55.2, 44.0, 36.9, 35.9, 35.8, 16.8, 2C are missing; IR (film): ν_{max} 2932, 1683, 1513, 1245 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{20}H_{24}NO_3$: 326.1756; found: 326.1763.

4.8.7. (3*RS*,5*RS*)-1-Benzyl-5-(furan-2-yl)-3-methylpyrrolidin-2-one 5i. Obtained according to procedure B. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.39 (s, 1H), 7.25 (m, 3H), 7.12 (d, 2H, $J = 7.3$ Hz), 6.34 (td, 1H, $J = 1.7$, 4.8 Hz), 6.21 (d, 1H, $J = 3.1$ Hz), 4.94 (d, 1H, $J = 14.7$ Hz), 4.43 (dd, 1H, $J = 7.1$, 8.1 Hz), 3.58 (d, 1H, $J = 14.7$ Hz), 2.53 (m, 2H), 1.87 (td, $J = 8.7$, 12.0 Hz, 1H), 1.34 (d, 3H, $J = 6.7$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 177.5, 152.4, 143.4, 137.1, 128.9, 128.8, 127.8, 110.7, 109.8, 53.5, 45.1, 36.9, 33.7, 17.0; IR (film): ν_{max} 2973, 2932, 1699 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{16}H_{18}NO_2$: 256.1338; found: 256.1342.

4.8.8. (3*RS*,5*RS*)-5-(4-Fluorophenyl)-3-methyl-1-phenylpyrrolidin-2-one 5j. Obtained according to procedure B. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.17 (m, 3H), 7.09–6.86 (m, 4H), 4.98 (d, 2H, $J = 14.4$ Hz), 4.18 (dd, 1H, $J = 7.0$, 8.5 Hz), 3.39 (d, 1H, $J = 14.5$ Hz), 2.50 (m, 2H), 1.41 (m, 1H), 1.25 (d, 3H, $J = 6.6$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 178.2, 164.9, 160.9, 136.7, 129.4, 129.0, 127.9, 116.4, 116.1, 59.7, 44.9, 38.8, 37.3, 16.9; ^{19}F NMR (235 MHz, $CDCl_3$): δ −114.3 (tt, $J = 8.2$, 5.6 Hz); IR (film) ν_{max}: 3444, 2931, 1691, 1511, 1407, 1225 cm^{-1}.

4.8.9. (3*RS*,5*RS*)-1-Benzyl-5-isopropyl-3-methylpyrrolidin-2-one 5k. Obtained according to procedure B. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.25 (m, 5H), 5.12 (d,

1H, $J = 14.9$ Hz), 3.79 (d, 1H, $J = 14.9$ Hz), 3.33 (ddd, 1H, $J = 3.9$, 7.3, 8.8 Hz), 2.47 (qt, 1H, $J = 7.1$, 9.1 Hz), 2.20–2.00 (m, 2H), 1.25 (d, 3H, $J = 7.1$ Hz), 1.25 (m, 1H), 0.81 (d, 3H, $J = 6.9$ Hz), 0.73 (d, 3H, $J = 6.8$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 178.7, 137.0, 128.9, 128.5, 127.8, 59.4, 44.5, 36.5, 26.9, 26.8, 18.7, 16.8, 14.2; IR (film): ν_{max} 2962, 2932, 1687, 1454, 1421, 701 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{15}H_{22}NO$: 232.1701; found: 232.1705.

4.8.10. (3*R*,5*S*)-1-Benzyl-3-methyl-5-pentylpyrrolidin-2-one 5l. Obtained according to procedure B. Yellow oil; $[\alpha]_D^{25} = -22.5$ (c 0.5, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.30 (t, 2H, $J = 7.1$ Hz), 7.26 (t, 1H, $J = 7.1$ Hz), 7.21 (d, 2H, $J = 6.9$ Hz), 4.98 (d, 1H, $J = 15.0$ Hz), 3.99 (d, 1H, $J = 15.0$ Hz), 3.30 (m, 1H), 2.47 (qdd, 1H, $J = 7.1$, 9.9, 14.1 Hz), 2.35 (ddd, 1H, $J = 6.7$, 8.8, 12.4 Hz), 1.26 (d, 3H, $J = 7.0$ Hz), 1.21 (m, 8H), 0.86 (t, 3H, $J = 6.9$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 178.3, 137.3, 128.9, 128.3, 127.7, 55.5, 44.6, 36.9, 34.4, 33.8, 32.2, 24.4, 22.9, 17.0, 14.9; IR (film): ν_{max} 2930, 2859, 1688, 1454, 1418, 700 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{17}H_{26}NO$: 260.2009; found: 260.2014.

4.8.11. (3*RS*,5*RS*)-3-Benzyl-1-(4-methoxybenzyl)-5-phenylpyrrolidin-2-one 5m. Obtained according to procedure B. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.35–7.15 (m, 10H), 6.94 (d, 2H, $J = 8.7$ Hz), 6.77 (d, 2H, $J = 8.7$ Hz), 5.02 (d, 1H, $J = 14.3$ Hz), 4.20 (dd, 1H, $J = 7.3$, 8.6 Hz), 3.77 (s, 3H), 3.40 (d, 1H, $J = 14.3$ Hz), 3.34 (dd, 1H, $J = 9.2$, 1.1 Hz), 2.87 (m, 2H), 2.76 (td, 2H, $J = 2.8$, 9.3 Hz), 2.37 (dt, 1H, $J = 7.6$, 13.0 Hz), 1.59 (ddd, 1H, $J = 8.9$, 9.8, 13.1 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 176.6, 159.3, 141.0, 139.7, 130.4, 129.5, 129.3, 128.9, 128.5, 127.6, 126.7, 114.2, 60.1, 55.6, 44.4, 44.3, 37.4, 35.6; IR (film): ν_{max} 2931, 1686, 1611, 1512, 1409, 1247, 701 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{25}H_{26}NO_2$: 372.1964; found: 372.1953.

4.9. General procedure for the preparation of amino alcohol 6

To a mixture of phenylglycinol-derived imine (3 mmol), zinc dust (0.49 g, 7.5 mmol), and $CeCl_3{\cdot}7H_2O$ (0.12 g, 0.5 mmol) in THF (15 mL), was added dropwise cinnamyl or crotylbromide (7.5 mmol) at 0 °C. The resulting mixture was stirred for 2 h and quenched with water (15 mL). The layers were separated and the aqueous layer extracted with Et_2O (3 × 10 mL). The organic layers were combined, dried over Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography on silica gel using a mixture of petroleum ether/AcOEt as solvent to give the corresponding amino alcohol.

4.9.1. (*R*)-2-[(1*R*,2*R*)-2-Methyl-1-phenylbut-3-enylamino]-2-phenylethanol 6a. Yellow oil; $[\alpha]_D^{25} = -23$ (c 1, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.30–7.08 (m, 10H), 5.68 (ddd, 1H, $J = 7.8$, 10.3, 17.3 Hz), 5.04 (dm, 1H, $J = 10.3$ Hz), 5.02 (dm, 1H, $J = 17.3$ Hz), 3.80–3.72 (m, 2H), 3.51 (dd, 1H, $J = 7.5$, 12.1 Hz), 2.61 (hex, 1H, $J = 6.8$ Hz), 2.35 (br s, 2H), 0.96 (d, 3H, $J = 6.9$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 141.5, 141.3, 140.3, 128.4, 128.0, 127.8, 127.3, 127.0, 126.9, 115.3, 65.0, 64.3, 60.8, 42.7, 16.6; IR (film): ν_{max} 3386, 1453, 1028, 758, 700 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{17}H_{23}N_2O$: 281.

4.9.2. (*R*)-2-[(2*R*,3*R*)-1-(Benzyloxy)-3-phenylpent-4-en-2-ylamino]-2-phenylethanol 6b. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.26 (m, 15H), 6.05 (ddd, 1H, $J = 9.5$, 10.1, 17.0 Hz), 5.14 (dm, 1H, $J = 17.0$ Hz), 5.11 (dm, 1H, $J = 10.1$ Hz), 4.21 (s, 2H), 3.61 (t, 1H, $J = 8.5$ Hz), 3.56 (dd, 1H, $J = 4.3$, 9.2 Hz), 3.44 (m, 2H), 3.27 (dd, 1H, $J = 4.2$, 9.1 Hz), 3.22 (dd, 1H, $J = 4.0$, 9.4 Hz), 2.99 (ddd, 1H, $J = 3.7$, 4.6, 8.3 Hz), 1.79 (br s, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 142.8, 138.8, 129.0, 128.9, 128.7, 128.5, 128.0, 127.9, 127.4, 126.9, 117.3, 73.4, 70.1, 66.9, 63.9, 60.6, 53.2; IR (film): ν_{max} 3395, 3028, 2864, 1495, 1453, 700 cm^{-1}.

4.9.3. 2-(1,2-Diphenylbut-3-enylamino)ethanol 6c. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.18 (m, 5H), 5.71 (ddd, 1H, $J = 8.0$, 10.2, 17.0 Hz), 4.77 (dm, 1H, $J = 10.2$ Hz), 4.64 (dm, 1H, $J = 17.0$ Hz), 3.79 (d, 1H, $J = 9.2$ Hz), 3.46 (dd, 1H, $J = 8.3$, 8.8 Hz), 3.35–3.17 (m, 2H), 2.41 (dd, 1H, $J = 4.7$, 12.7 Hz), 2.33 (dd, 1H, $J = 4.7$, 12.7 Hz), 2.07 (br s, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 141.5, 141.3, 138.6, 128.7, 128.25, 128.2, 128.1, 127.3, 126.8, 116.4, 67.1, 60.8, 57.3, 48.7; IR (film): ν_{max} 3328, 3027, 2921, 1493, 1453, 1055, 756, 701 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{18}H_{22}NO$: 268.1701; found: 268.1709.

4.9.4. (*R*)-2-[(3*S*,4*R*)-2-Methyl-4-phenylhex-5-en-3-ylamino]-2-phenylethanol 6d. Yellow oil; $[\alpha]_D = -123$ (c 0.5, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.34 (m, 8H), 7.15 (dd, 2H, $J = 1.8$, 7.8 Hz), 5.96 (td, 1H, $J = 9.9$, 17.0 Hz), 5.09 (dm, 1H, $J = 17.0$ Hz), 5.06 (dm, 1H, $J = 10.0$ Hz), 3.42 (t, 1H, $J = 8.9$ Hz), 3.35–3.24 (m, 3H), 2.68 (dd, 1H, $J = 3.2$, 8.2 Hz), 1.84 (hept d, 1H, $J = 3.1$, 6.9 Hz), 0.85 (d, 3H, $J = 6.8$ Hz), 0.66 (d, 3H, $J = 6.7$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 143.6, 141.5, 139.9, 128.5, 128.3, 128.2, 127.7, 127.4, 126.5, 115.5, 66.7, 63.9, 63.2, 55.6, 29.7, 21.0, 15.9.

4.9.5. (*R*)-2-[(1*R*,2*R*)-1-(Furan-2-yl)-2-phenylbut-3-enylamino]-2-phenylethanol 6e. Yellow oil; $[\alpha]_D^{25} = -15$ (c 0.5, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.35–7.15 (m, 9H), 7.05 (d, 2H, $J = 7.7$ Hz), 6.14 (dd, 1H, $J = 1.8$, 3.1 Hz), 5.97 (ddd, 1H, $J = 8.4$, 10.4, 18.8 Hz), 5.91 (m, 1H), 5.00 (dm, 1H, $J = 10.4$ Hz), 4.97 (dm, 1H, $J = 18.8$ Hz), 3.96 (d, 1H, $J = 8.7$ Hz), 3.74 (t, 1H, $J = 8.5$ Hz), 3.58 (m, 2H), 3.35 (td, 1H, $J = 3.6$, 9.3 Hz), 1.99 (br s, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 154.5, 141.8, 141.5, 141.3, 138.1, 128.7, 128.4, 128.2, 127.3, 127.0, 126.9, 117.0, 109.9, 108.2, 65.3, 62.4, 59.4, 55.2; IR (film): ν_{max} 3332, 3028, 1453, 1071, 756, 700 cm^{-1}.

4.10. General procedure for the preparation of pyrrolidinone 7

4.10.1. (*R*)-3-[(1*R*,2*S*)-2-Methyl-1-phenylbut-3-enyl]-4-phenyloxazolidin-2-one 7a. Obtained according to procedure A. Yellow solid; mp 76 °C; $[\alpha]_D^{25} = -5.5$ (c 1.4, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.37 (m, 4H), 7.27 (m, 6H), 5.38 (ddd, 1H, $J = 7.6$, 10.2, 17.0 Hz), 4.77 (dm, 1H,

$J = 17.0$ Hz), 4.75 (dm, 1H, $J = 10.2$ Hz), 4.59 (dm, 1H, $J = 11.8$ Hz), 4.42 (dd, 1H, $J = 8.0$, 8.9 Hz), 4.31 (dd, 1H, $J = 7.2$, 8.9 Hz), 4.11 (dd, 1H, $J = 7.2$, 8.0 Hz), 2.53 (qdd, 1H, $J = 6.5$, 7.6, 11.8 Hz), 1.14 (d, 3H, $J = 6.5$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 158.8, 140.6, 138.6, 137.2, 129.6, 129.1, 128.8, 128.2, 128.0, 127.9, 115.2, 70.1, 64.5, 59.8, 38.1, 18.3; IR (film): ν_{max} 2975, 2927, 1748, 1400, 1222, 1059, 707 cm^{-1}; HRMS-ESI: m/z $[M+Na]^+$ calcd for $C_{20}H_{21}NO_2Na$: 330.1470; found: 330.1475.

4.10.2. (*R*)-3-[(2*R*,3*R*)-1-(Benzyloxy)-3-phenylpent-4-en-2-yl]-4-phenyloxazolidin-2-one 7b. Obtained according to procedure A. Yellow oil; $[\alpha]_D^{25} = -102$ (c 1.3, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.32 (m, 9H), 7.15 (m, 4H), 7.01 (d, 2H, $J = 7.2$ Hz), 5.85 (ddd, 1H, $J = 7.8$, 10.1, 16.9 Hz), 5.06 (dd, 1H, $J = 1.3$, 16.9 Hz), 4.98 (dd, 1H, $J = 1.3$, 10.1 Hz), 4.47 (d, 1H, $J = 11.5$ Hz), 4.41 (d, 1H, $J = 11.5$ Hz), 4.14 (m, 1H), 4.12 (t, 1H, $J = 8.4$ Hz), 3.81 (t, 1H, $J = 8.5$ Hz), 3.75–3.63 (m, 4H); ^{13}C NMR δ 158.6, 142.0, 138.9, 138.6, 137.7, 129.3, 128.8, 128.6, 128.4, 128.2, 127.6, 117.1, 73.5, 70.8, 69.5, 62.0, 58.3, 50.9; IR (film): ν_{max} 3030, 2907, 2248, 1714, 1418, 1097 cm^{-1}.

4.10.3. (3*SR*,4*RS*,5*RS*)-3-(1,2-Diphenylbut-3-enyl)oxazolidin-2-one 7c. Obtained according to procedure A. Colorless oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.52–7.12 (m, 10H), 5.78 (ddd, 1H, $J = 7.3$, 10.4, 17.1 Hz), 5.36 (d, 1H, $J = 12.1$ Hz), 4.93 (dm, 1H, $J = 10.4$ Hz), 4.88 (dm, 1H, $J = 17.1$ Hz), 4.14 (ddm, 1H, $J = 7.3$, 12.1 Hz), 3.98 (ddd, $J = 5.1$, 8.4, 9.2 Hz, 1H), 3.77 (q, 1H, $J = 8.5$ Hz), 3.34 (ddd, $J = 5.1$, 8.0, 9.0 Hz, 1H), 3.23 (dd, 1H, $J = 8.3$, 17.4 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 157.5, 140.0, 138.2, 136.8, 128.75, 128.70, 128.4, 128.1, 127.8, 127.0, 117.2, 77.0, 61.6, 59.7, 50.5, 40.4; IR (film): ν_{max} 3031, 2976, 1750, 1458, 1401; 1223, 1059, 706 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{19}H_{20}NO_2$: 294.1494; found: 294.1500.

4.10.4. (*R*)-3-[(3*S*,4*R*)-2-Methyl-4-phenylhex-5-en-3-yl]-4-phenyloxazolidin-2-one 7d. Obtained according to procedure A. Yellow oil; mp 110 °C; $[\alpha]_D^{25} = -219$ (c 1, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.32 (m, 8H), 7.12 (m, 2H), 5.96 (ddd, 1H, $J = 9.9$, 10.0, 16.9 Hz), 5.16 (dm, 1H, $J = 16.9$ Hz), 5.02 (dm, 1H, $J = 10.0$ Hz), 4.19 (t, 1H, $J = 10.1$ Hz), 4.01 (dd, 1H, $J = 8.0$, 13.7 Hz), 3.94 (dd, 1H, $J = 7.8$, 13.7 Hz), 3.61 (dd, 1H, $J = 7.8$, 8.0 Hz), 3.15 (dd, 1H, $J = 4.1$, 10.8 Hz), 2.11 (m, 1H), 0.94 (d, 3H, $J = 7.0$ Hz), 0.66 (d, 3H, $J = 6.8$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 158.1, 142.6, 139.1, 137.8, 129.0, 128.7, 128.6, 128.4, 128.0, 126.8, 116.2, 69.3, 64.4, 63.2, 50.8, 30.6, 21.7, 19.4; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{22}H_{26}NO_2$: 336.1964; found: 336.1971.

4.11. *tert*-Butyl benzyl[(1*R*,2*R*)-1-(furan-2-yl)-2-phenylbut-3-enyl]carbamate 7e

To a solution of $Pb(OAc)_4$ (540 mg,1.2 mmol) in MeOH (5 mL) was added a solution of **6e** (333 mg, 1 mmol) in CH_2Cl_2 (5 mL) at 0 °C and the resulting mixture was stirred for 1 h. CH_2Cl_2 (10 mL) was added followed by water (10 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under vacuum. The residue was dissolved in MeOH (5 mL) then $NaBH_4$ (35 mg, 0.9 mmol) was added in small portions at 0 °C. The reaction was stirred for 1 h at rt and quenched by adding water (10 mL). The aqueous layer was extracted with Et_2O (3 × 15 mL), the organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under vacuum, to give the expected amino alcohol, which was used in the next step without purification: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.44–7.20 (m, 7H), 7.11 (dd, 2H, $J = 2.0$, 6.7 Hz), 7.03 (dd, 2H, $J = 2.0$, 7.9 Hz), 6.33 (dd, 1H, $J = 1.8$, 3.1 Hz), 6.17 (d, $J = 3.1$ Hz, 1H), 5.84 (ddd, 1H, $J = 8.1$, 10.3, 17.0 Hz), 4.90 (dm, 1H, $J = 10.3$ Hz), 4.85 (dm, 1H, $J = 17.0$ Hz), 3.91 (d, 1H, $J = 9.3$ Hz), 3.77 (d, 1H, $J = 8.4$ Hz), 3.69 (d, 1H, $J = 13.8$ Hz), 3.42 (d, 1H, $J = 13.8$ Hz), 1.66 (br s, 2H). To a solution of the crude amine and DMAP (12 mg, 0.1 mmol) in CH_2Cl_2 (3 mL) was added dropwise a solution of $(Boc)_2O$ (275 mg, 1.25 mmol) in CH_2Cl_2 (2 mL) at rt. The reaction mixture was then stirred for 4 h at rt. and quenched by adding water (2 mL). The aqueous layer was extracted with dichloromethane (3 × 5 mL), the organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under vacuum. The residue was purified by column chromatography on silica gel using a mixture of petroleum ether/AcOEt as eluant to give **7e**. $[\alpha]_D^{25} = +62$ (c 1.1, CH_2Cl_2); 4:1 mixture of rotamers, major isomer ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.06 (s, 9H), 4.03 (d, 1H, $J = 16.1$ Hz), 4.12 (dd, 1H, $J = 11.6$, 7.2 Hz), 4.34 (d, 1H, $J = 16.1$ Hz), 4.93 (br d, 1H, $J = 10.9$ Hz), 4.94 (br d, 1H, $J = 16.5$ Hz), 5.94–5.80 (m, 2H), 6.26 (br s, 1H), 6.37 (br s, 1H), 6.67 (m, 2H), 6.67 (br m, 2H), 7.29 (m, 7H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 155.3, 152.7, 141.7, 140.3, 139.5, 138.6, 128.3 (2C), 127.6, 126.6, 126.3, 126.0, 116.4, 100.1, 109.1, 79.6, 55.6, 51.7, 47.6, 27.9; IR (film): ν_{max} 2977, 1690, 1453, 1403, 1366, 1248, 1165 cm^{-1}; MS-ESI: m/z $[M+H]^+$: 404.

4.12. Preparation of pyrrolidinones 8

4.12.1. (3*S*,4*S*,5*R*)-1-[(*R*)-2-Hydroxy-1-phenylethyl]-3,4-dimethyl-5-phenylpyrrolidin-2-one 8a. Obtained according to procedure B. Yellow oil; $[\alpha]_D^{25} = -38$ (c 0.6, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.30 (m, 6H), 7.12 (m, 4H), 5.41 (dd, 1H, $J = 8.0$, 6.4 Hz), 4.13 (d, 1H, $J = 8.3$ Hz), 3.71 (m, 3H), 2.95 (br s, 1H), 2.41 (qd, $J = 6.9$, 13.7 Hz, 1H), 2.07 (qdd, 1H, $J = 6.9$, 8.2, 11.7 Hz), 1.19 (d, 3H, $J = 6.9$ Hz), 0.54 (d, 3H, $J = 6.8$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 178.6, 138.3, 136.3, 128.5, 128.4 (3C), 128.0, 127.9, 63.7, 62.95, 62.9, 58.7, 41.9, 41.6, 14.2, 13.7; IR (film): ν_{max} 3438, 29.64, 1454, 1421, 701 cm^{-1}.

4.12.2. (3*S*,4*R*,5*R*)-5-(Benzyloxymethyl)-1-[(*R*)-2-hydroxy-1-phenylethyl]-3-methyl-4-phenylpyrrolidin-2-one 8b. Obtained according to procedure B. Yellow oil; $[\alpha]_D^{25} = -60$ (c 0.6, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.31 (m, 11H), 7.20 (d, 2H, $J = 6.9$ Hz), 7.11 (d, 2H, $J = 7.7$ Hz), 5.08 (dd, 1H, $J = 4.5$, 7.9 Hz), 4.24 (dd, 1H, $J = 6.8$, 12.0 Hz), 4.19 (m, 1H), 4.12 (dd, 1H, $J = 4.6$, 12.0 Hz), 3.92 (d, 1H, $J = 11.2$ Hz), 3.86 (d, 1H, $J = 11.2$ Hz), 3.52

(dm, 1H, $J = 7.3$ Hz), 3.33–3.29 (m, 2H), 3.18 (dd, 1H, $J = 2.9$, 10.4 Hz), 2.86 (d, 1H, $J = 10.4$ Hz), 1.19 (d, 3H, $J = 6.4$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 178.8, 137.3, 137.1, 136.5, 128.6, 128.5, 128.4, 128.3, 127.8, 127.7, 127.7, 127.2, 73.1, 68.1, 64.0, 61.9, 60.7, 51.7, 39.8, 14.5; IR (film): ν_{max} 3330, 1490, 1450, 1300, 1050, 705 cm^{-1}.

4.12.3. 1-(2-Hydroxyethyl)-3-methyl-4,5-diphenylpyrrolidin-2-one 8c. Obtained according to procedure B. Yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.10 (m, 6H), 6.75 (m, 4H), 4.86 (d, 1H, $J = 8.2$ Hz), 3.80 (m, 3H), 3.61 (dd, 1H, $J = 8.2$, 11.7 Hz), 3.37 (br t, 1H $J = 4.6$ Hz), 3.14 (m, 1H), 2.96 (dd, 1H, $J = 6.8$, 11.4 Hz), 1.20 (d, 3H, $J = 6.9$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 178.7, 136.3, 136.0, 128.3, 128.2, 128.0, 127.8, 127.1, 127.0, 67.2, 61.5, 53.8, 46.2, 38.8, 13.8.

4.12.4. (3*S*,4*S*,5*R*)-1-[(*R*)-2-Hydroxy-1-phenylethyl]-4-isopropyl-3-methyl-5-phenylpyrrolidin-2-one 8d. Obtained according to procedure B. White solid; mp 150 °C; $[\alpha]_D^{25} = -75$ (c 0.4, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.44–7.22 (m, 10H), 4.64 (dd, 1H, $J = 4.1$, 8.1 Hz), 4.37 (dt, 1H, $J = 7.9$, 11.3 Hz), 4.09 (td, 1H, $J = 3.9$, 15.1 Hz), 3.82 (dd, 1H, $J = 4.1$, 7.8 Hz), 3.65 (dd, 1H, $J = 2.1$, 8.4 Hz), 3.53 (dd, 1H, $J = 8.4$, 12.7 Hz), 3.26 (quint, 1H, $J = 6.6$ Hz), 1.59 (m, 1H), 1.24 (d, 3H, $J = 6.7$ Hz), 0.67 (d, 3H, $J = 7.2$ Hz), 0.37 (d, 3H, $J = 7.1$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 179.3, 137.8, 136.7, 128.5, 128.5, 128.1, 127.6, 127.1, 70.4, 65.3, 65.0, 52.5, 39.0, 30.5, 19.1, 17.7, 14.7; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{22}H_{28}NO_2$: 338.2120; found: 338.2116.

4.12.5. (3*S*,4*S*,5*R*)-1-Benzyl-5-(2-furyl)-4-phenylpyrrolidin-2-one 8e. Obtained and isolated according to procedure B as a mixture 4.5/1 of diastereomers as a pale yellow oil; $[\alpha]_D^{25} = -216$ (c 0.3, CH_2Cl_2); Main isomer: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.40–7.10 (m, 9H), 6.91 (dd, 2H, $J = 1.8$, 7.2 Hz), 6.15 (dd, 1H, $J = 1.6$, 3.2 Hz), 5.92 (d, 1H, $J = 3.2$ Hz), 5.17 (d, 1H, $J = 14.8$ Hz), 4.55 (d, 1H, $J = 7.2$ Hz), 3.63 (d, 1H, $J = 14.8$ Hz), 3.30–3.14 (m, 2H), 1.26 (d, 3H, $J = 6.4$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 176.5, 149.9, 142.5, 136.5, 128.7, 128.3, 128.1, 127.9, 127.6, 127.1, 110.1, 109.7, 58.6, 52.6, 45.0, 39.5, 14.2, 1C is missing; IR (film): ν_{max} 2931, 1696, 1497, 1454, 1232, 755, 700 cm^{-1}; HRMS-ESI: m/z $[M+H]^+$ calcd for $C_{12}H_{22}NO_2$: 332.1651; found: 332.1655.

Acknowledgment

We thank the CNRS and the Ministère de l'Education Nationale for their financial support.

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