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Diastereoselective Access to Enantiomerically Pure *cis*-2,3-Disubstituted Pyrrolidines

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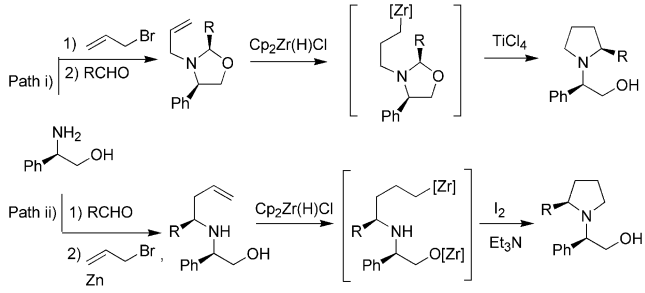
A straightforward access to enantiomerically pure 2,3-disubstituted pyrrolidines is reported that involves diastereoselective allylation of (*R*)-phenylglycinol-derived imines and a sequential hydrozirconation–cyclization. A number of pyrrolidine derivatives bearing aryl, heteroaryl, alkyl and alkenyl groups have been prepared in this way. Such compounds are useful building blocks in the synthesis of molecules of biological interest, as illustrated by the syntheses of proline derivatives and the naturally occurring alkaloid (–)-isoretronecanol.

Introduction

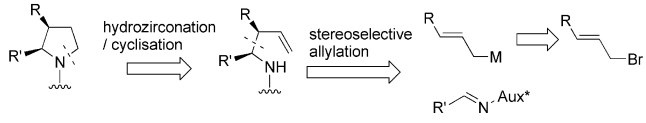
The pyrrolidine ring system is common to a number of naturally occurring[1] and medicinally important compounds.[2] Furthermore, optically pure pyrrolidines are widely used as chiral inductors and organocatalysts in asymmetric synthesis.[3] Although numerous syntheses of substituted pyrrolidines have been reported,[4] there is a continued need for simple and efficient methods that provide a stereocontrolled access to optically pure compounds. Of the pyrrolidines synthesized, *cis*-2,3-disubstituted pyrrolidines are valuable building blocks for the preparation of numerous bioactive molecules that possess pyrrolidine rings and are thus attractive synthetic targets. Surprisingly, there is a lack of general synthetic methods available for synthesizing 2,3-disubstituted pyrrolidines and a simple asymmetric access to such compounds would be of significant interest.[5]

We recently reported a hydrozirconation-based methodology for the asymmetric construction of five- and six-membered N-heterocycles.[6] Among the reactions described, a selective preparation of both enantiomeric 2-substituted pyrrolidines was achieved by using the same starting materials (allyl bromide and an aldehyde) and (*R*)-phenylglycinol as the chiral inductor (Scheme 1). The sequence in pathway (i) proceeds via *N*-allyloxazolidines and involves hydrozirconation–Lewis acid mediated cyclization. The preparation of the second enantiomer was based on our finding that alkene hydrozirconation can be performed in the presence of a secondary amino group; the one-pot sequence in pathway (ii) involves the hydrozirconation–iodination of homoallylic amines.[6b]



Scheme 1. Zirconium-mediated synthesis of 2-substituted pyrrolidines.

We assumed that 2,3-disubstituted pyrrolidines could be synthesized according to pathway (ii).[7] In this case, the stereochemistry would be controlled by diastereoselective allylation of phenylglycinol-derived imines, as shown in Scheme 2.



Scheme 2. Retrosynthetic approach to 2,3-disubstituted pyrrolidines.

Although the addition of allylic organometallic compounds to chiral imines is well known,[8] such reactions are often capricious in terms of yield and selectivity and much more difficult to control in comparison with those involving aldehydes. For example, only a few methods are applicable to enolizable aldimines. There is still a need to increase substrate scope, particularly in the organometallic part, which

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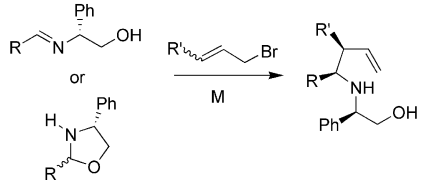
would provide wider access to optically active amines. Among the metals known to promote the allylation of chiral imines, zinc and indium have emerged as attractive candidates: (i) branched regioisomeric homoallylic amines typically predominate over linear amines with these metals and (ii) the required *syn* stereoselectivity and good diastereofacial selectivity may be achieved.[9] Herein we demonstrate that the Barbier-type allylation of optically active phenylglycinol-derived aldimines proceeded with high regio- and stereoselectivity.

Results and Discussion

Two different Barbier-type protocols were selected for the preparation of the desired unsaturated amines. First, a mixture of imine and bromide was added to a suspension of zinc in the presence of a catalytic amount of $CeCl_3 \cdot 7H_2O$ in THF following the procedure of Umano-Ronchi and coworkers.[10] This method was successfully applied to imines derived from aromatic aldehydes to afford good yields and stereoselectivities (Table 1, Method A). With substrates derived from aliphatic aldehydes, however, the *N*-alkyl product was competitively formed. This side-reaction possibly originates from the preferential formation of oxazolines instead of imines when condensing phenylglycinol and aliphatic aldehydes. Whereas the zinc-based protocol appears to be limited to aromatic or α,β-unsaturated imines, the use of indium in MeOH to generate the allylmetal species[9b] allowed this side-reaction to be overcome, leading to the expected amines in good-to-moderate yields (Method B).

By applying Method A or B, homoallylic amines bearing aromatic, heteroaromatic, alkyl or alkenyl groups were obtained, most of them being isolated in diastereomerically pure form after purification by column chromatography (Table 1). Different combinations of substituents, that is, two aryls or heteroaryls (entries 1 and 2), 2-aryl or 2-heteroaryl and 3-alkyl (entries 3 and 4), alkenyl and alkyl (entries 5 and 6) or two alkyls (entries 8–15), were achieved. The method also allows the incorporation of structural fragments including variously protected alcohols (entries 3–15) or amines (in this case, the low isolated yield originates from the problematic isomeric separation, entry 15). Interestingly, homoallylic amines **1j** and **1k** bearing reversed alcohol protection (OTBS and OBn) can be prepared (entries 10 and 11). The only limitation was observed in the case of 2-alkyl and 3-aryl (entry 7) for which low selectivity and yield were obtained by methods A and B. Branched regioisomers were solely obtained irrespective of the procedure employed. Only *syn* stereoisomers were formed in typically high diastereomeric ratios. The reaction proceeded with unvarying and high stereoselectivity regardless of the C=C double bond configuration in the alkenyl bromide (entries 11 and 12). The disubstituted homoallylic amine **1k** was obtained in good yield and stereoselectivity, according to the NMR spectrum of the crude product, and isolated as a single isomer. The preferential formation of *syn* rather than *anti* stereoisomers presumably arises from a Traxler–Zimmermann-type transition state in which the metal is coordinated to both the N and the O atoms of the imine. In this case, the imine substituents adopt a pseudo-axial

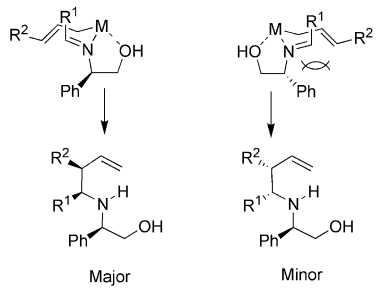
Table 1. Indium- and zinc-mediated diastereoselective allylation of phenylglycinol-derived imines.



Entry	R	R′	Alkene/Method[a]	Compound, *dr* (% yield)[b]
1	2-furyl	Ph	*E*/A	**1a**, 11:1 (86)
2	3-pyridyl	Ph	*E*/A	**1b**, 9.7:1 (91)[c]
3	2-furyl	$TBSOCH_2$	*Z*/A	**1c**, 10.7:1 (75)
4	Ph	$TBSOCH_2$	*Z*/A	**1d**, 9.2:1(85)[d]
5	cinnamyl	$BnOCH_2$	*Z*/B	**1e**, 14:1 (64)
6	cinnamyl	$TBSOCH_2$	*Z*/B	**1f**, 13:1 (83)
7	$BnOCH_2$	Ph	*Z*/B	**1g**, 2:1 (37)
8	$BnOCH_2$	n-C_5H_{11}	*Z*/B	**1h**, 5:1 (74)
9	*i*Bu	$BnOCH_2$	*Z*/B	**1i**, 11:1(54)[e]
10	$BnO(CH_2)_3$	$TBSOCH_2$	*Z*/B	**1j**, 10:1(49)
11	$TBSO(CH_2)_3$	$BnOCH_2$	*Z*/B	**1k**, 8:1 (71)
12	$TBSO(CH_2)_3$	$BnOCH_2$	*E*/B	**1k**, 9:1 (75)
13	n-C_6H_{13}	$TBSOCH_2$	*Z*/B	**1l**, 17:1 (70)
14	CH_3	$BnOCH_2$	*Z*/B	**1m**, 7.6:1 (55)[f]
15	$BocNBn(CH_2)_2$	$BnOCH_2$	*Z*/B	**1n**, 3:1 (30)

[a] Reagents and conditions: Method A: imine (1 mmol), bromide (2.5 mmol), Zn (2.5 mmol) and $CeCl_3 \cdot 7H_2O$ (0.1 mmol) in THF (10 mL), room temp., 4 h; method B: imine (1 mmol.), bromide (1.2 mmol) and In (1 mmol) in MeOH (5 mL), room temp., 4 h. [b] Isolated yield of the major diastereomer in diastereomerically pure form. [c] Isolated as a 20:1 mixture of diastereomers. [d] Inseparable mixture of diastereoisomers. [e] Isolated as a 25:1 mixture of diastereomers. [f] Isolated as a 11:1 mixture of diastereomers.

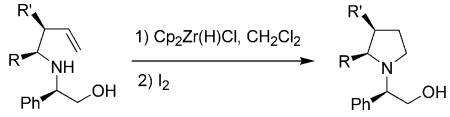
position, which, associated with the equatorial orientation of the allylmetal substituent, preferentially give the *syn* adduct. The generally high level of facial diastereoselectivity observed can be explained by assuming an efficient discrimination between the two diastereoisomeric pseudo-chair-like transition states (Scheme 3).



Scheme 3. Stereochemical outcome of the allylation reaction.

With the aforementioned substrates in hand, the pyrrolidine ring was next constructed through the one-pot hydrozirconation–iodination sequence (Table 2). These reactions were carried out in CH_2Cl_2 at room temperature according to the previously described protocol.[6] In the present case, however, 3 (and not 2) equiv. of the Schwartz reagent were required to achieve the complete hydrozirconation of the alkene. Several 2,3-disubstitued pyrrolidines were prepared on the gram scale and isolated in good yields as a single stereoisomer (Table 2). The method appeared to be quite general, that is, pyrrolidines bearing an aryl and an heteroaryl (entry 1), a combination of alkyl and aryl or heteroaryl (entries 2 and 3) or two alkyl (entries 4–10) groups were prepared. Protected alcohol or amine functions could also be incorporated.

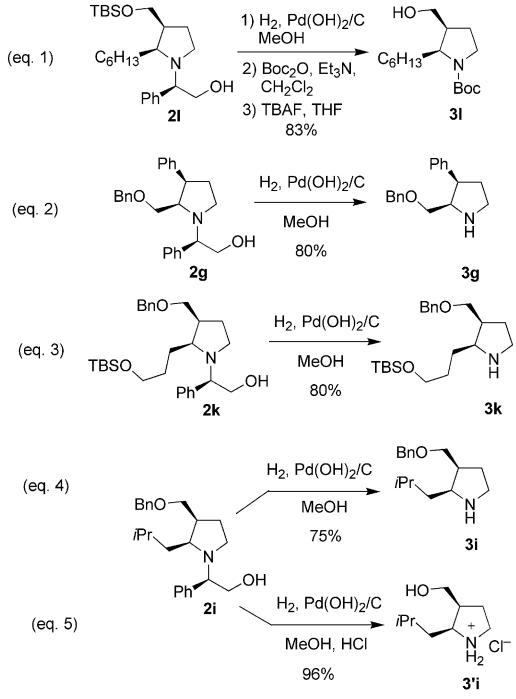
Table 2. Synthesis of 2,3-disubstituted pyrrolidines.



Entry	R	R′	Product	% Yield
1	2-furyl	Ph	**2a**	75
2	2-furyl	$TBSOCH_2$	**2c**	75
3	$BnOCH_2$	Ph	**2g**	77
4	$BnOCH_2$	C_5H_{11}	**2h**	67
5	*i*Bu	$BnOCH_2$	**2i**	71[a]
6	$BnO(CH_2)_3$	$TBSOCH_2$	**2j**	47
7	$TBSO(CH_2)_3$	$BnOCH_2$	**2k**	64
8	*n*-C_6H_{13}	$TBSOCH_2$	**2l**	63
9	CH_3	$BnOCH_2$	**2m**	66[b]
10	$BocNBn(CH_2)_2$	$BnOCH_2$	**2n**	58

[a] Isolated in diastereomerically pure form starting from a 25:1 mixture of diastereomers. [b] Isolated as a 13:1 mixture of diastereomers in diastereomerically pure form starting from a 9:1 mixture of diastereomers.

To obtain valuable pyrrolidine building blocks, we next focused our attention on the removal of the chiral auxiliary. In the case of pyrrolidines bearing an alkyl moiety at the 2-position, the phenylglycinol residue can be easily removed by $Pd(OH)_2$-catalysed hydrogenolysis [Equations (1)–(5) of Scheme 4]. Interestingly, depending upon the hydrogenolysis conditions applied, those pyrrolidines with an additional benzyloxy group can undergo selective debenzylation at the nitrogen [Equations (2)–(4)] or both benzylic units can be removed [Equation (5)].



Scheme 4. Removal of the chiral auxiliary.

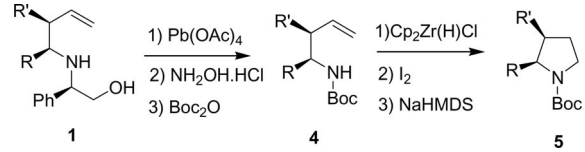
With pyrrolidines bearing an aromatic fragment at the 2-position, the hydrogenolysis deprotection conditions proved to be prohibited. In these cases, the chiral auxiliary was removed prior to cyclization under oxidative conditions by treating the allylation adduct with $Pb(OAc)_4$ followed by hydroxylamine transimination.[9b] The resulting primary amine was Boc-protected and next subjected to the hydrozirconation–halogenation sequence. Cyclization of the resulting iodocarbamate was promoted by the addition of NaHMDS[11] to give the Boc-protected 2,3-disubstituted pyrrolidines **5b–f** (Table 3).

According to this modified strategy, 2,3-disubstituted *N*-Boc-protected pyrrolidines containing aryl (entries 1 and 3), heteroaryl (entries 1 and 2) or even an alkenyl fragment (entries 4 and 5) at the 2-position were obtained in good yields.

cis-2,3-Disubstituted pyrrolidines can be considered as useful building blocks for the synthesis of a broad range of bioactive molecules. As examples, 3-substituted proline **6f** and 2-substituted β-prolines **6d** and **6l** were easily prepared by $RuCl_3$-catalysed oxidation of hydroxymethyl or styryl groups (Scheme 5). Compound **6f** is an orthogonally protected homoserine-constrained analogue.

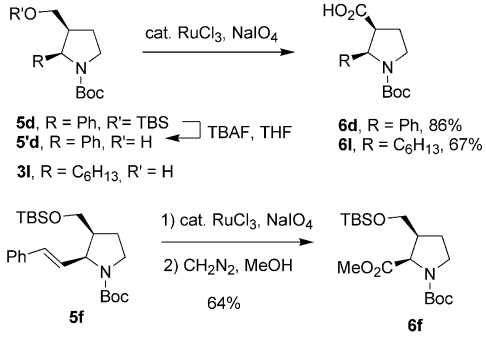
To illustrate the potential of the method in the field of alkaloid synthesis, short stereoselective syntheses of (–)-isoretronecanol[12] and an indolizidine, a homologue of plateniceyne, were carried out. In the first case, the pyrrolidine

Table 3. Synthesis of Boc-protected 2,3-dusbstituted pyrrolidines with 2-aryl or 2-alkenyl groups.



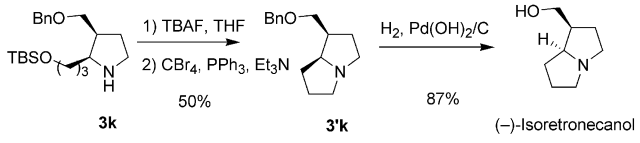
Entry	R	R′	% Yield of **4**	% Yield of **5**
1	3-pyridyl	Ph	**4b** (58)[a]	**5b** (48)[a]
2	2-furyl	$TBSOCH_2$	**4c** (65)	**5c** (52)
3	Ph	$TBSOCH_2$	**4d** (73)	**5d** (68)[b]
4	cinnamyl	$BnOCH_2$	**4e** (72)	**5e** (77)
5	cinnamyl	$TBSOCH_2$	**4f** (86)	**5f** (90)

[a] Obtained starting from a 20:1 mixture of diastereomers, *ee* = 90%. [b] Obtained starting from a 9.2:1 mixture of diastereomers, *ee* = 80%.



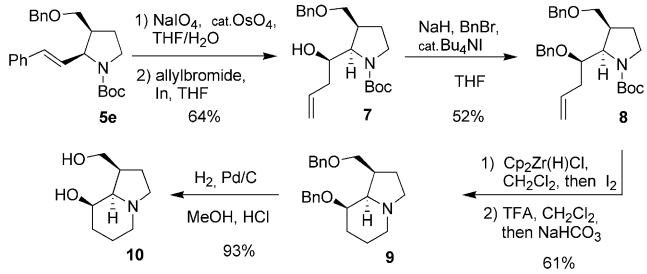
Scheme 5. Access to substituted proline and β-proline analogues.

3k was subjected to TBAF desilylation to give the corresponding amino alcohol. Subsequent conversion of the hydroxy group to the bromide promoted a spontaneous cyclization to afford the bicyclic **3′k**, which, after OBn deprotection, provided the optically pure (–)-isoretronecanol in 43% overall yield starting from **3k** (Scheme 6).



Scheme 6. Synthesis of (–)-isoretronecanol.

The indolizidine skeleton can also be constructed, as illustrated by the synthesis of the six-membered homologue of platynecine. The synthesis started from the pyrrolidine **5e** bearing a masked aldehyde function at the 2-position and a protected 3-hydroxymethyl chain (Scheme 7). Generation of the prolinecarbaldehyde skeleton was achieved by OsO_4-catalysed oxidation of the styryl moiety. The crude aldehyde underwent indium-mediated allylation to give **7** in 64% yield over two steps as a separable 8:1 mixture of diastereomers.[13,14] The alcohol function was then protected as a benzyloxy group. The hydrozirconation–iodination sequence was applied to the major isomer **8** to afford the intermediate iodopyrrolidine, which, after removal of the Boc group, spontaneously cyclized to give the bicycle **9**. Further hydrogenolysis under acidic conditions provided the target compound **10**[15] in 19% overall yield starting from **5e**. Note that two successive hydrozirconation steps were involved in the synthesis of **10** when considering the homoallylic amine **4e** as the precursor.



Scheme 7. Synthesis of (–)-indolizidine **10**.

Conclusions

We have reported a convenient stereoselective access to 2,3-disubstituted pyrrolidines based on chiral imine diastereoselective allylation and sequential hydrozirconation–cyclization, most of the products being isolated in an enantiomerically pure form. The methodology can be applied to the synthesis of a broad range of compounds bearing a combination of aryl, heteroaryl, alkyl and alkenyl groups. It offers a straightforward asymmetric entry to bioactive molecules possessing a pyrrolidine ring, as exemplified with a short synthesis of α- and β-proline derivatives as well as the naturally occurring (–)-isoretronecanol.

Experimental Section

General: All reactions were conducted under argon. Prior to use, THF and Et_2O were distilled under argon from sodium benzophenone ketyl, and Et_3N and CH_2Cl_2 were distilled under argon from CaH_2. $Cp_2Zr(H)Cl$ was prepared according to a known procedure.[16] ^1H and ^{13}C NMR spectra were recorded at 25 °C in $CDCl_3$, unless specified otherwise.

General Procedure for the Preparation of Homoallylic Amines (Method A): A solution of imine (1 mmol) and bromide (2.5 mmol) in THF (5 mL) was added dropwise to a suspension of Zn (158 mg, 2.5 mmol) and $CeCl_3{\cdot}7H_2O$ (37 mg, 0.1 mmol) in THF (5 mL) at room temp. The reaction mixture was stirred at room temp. for 4 h and then quenched with H_2O (10 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL). The organic phases were combined, dried with $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with a mixture of PE/AcOEt to give the corresponding amine.

(2*R*)-2-{[(1*R*,2*R*)-1-(2-Furyl)-2-phenylbut-3-en-1-yl]amino}-2-phenylethanol (1a): Obtained as an 11:1 mixture of diastereomers and isolated in pure diastereomerically pure form as a yellow oil (286 mg, 86%). $[\alpha]_D^{20} = -31.8$ (c = 1, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = 1.75 (br. s, 1 H, NH), 2.20 (br. s, 1 H, OH), 3.36 (dd, $^2J_{H,H}$ = 12.1, $^3J_{H,H}$ = 8.1 Hz, 1 H, CH_AH$_B$OH), 3.54–3.62 (m, 2 H, CH$_A$$H_BOH, CH$CH=CH$_2$), 3.74 (t, J = 8.5 Hz, 1 H, PhCHNH), 3.96 (d, $^3J_{H,H}$ = 8.5 Hz, 1 H, FurCHNH), 4.97 (d, $^3J_{H,H}$ = 17.9 Hz,

1 H, CH=CH_AH_B), 4.99 (d, $^3J_{H,H}$ = 9.9 Hz, 1 H, CH=CH$_A$$H_B$), 5.88–6.02 (m, 2 H, C$H$=CH$_2$, furyl 3-H), 6.14 (dd, $^3J_{H,H}$ = 3.1, 1.8 Hz, 1 H, furyl 4-H), 7.04 (dd, $^3J_{H,H}$ = 7.6, $^4J_{H,H}$ = 1.9 Hz, 2 H), 7.15–7.53 (m, 9 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 55.5, 59.7, 62.7, 65.5, 108.4, 110.1, 117.2, 127.2, 127.3, 127.6, 128.5, 128.7, 129.0, 138.3, 141.5, 141.8, 142.1 ppm. HRMS (ESI): calcd. for $C_{22}H_{23}NO_2Na$ [M + Na]$^+$ 356.1626; found 356.1633.

(2*R*)-2-Phenyl-2-{[(1*R*,2*R*)-2-phenyl-1-pyridin-3-ylbut-3-en-1-yl]-amino}ethanol (1b): Obtained as a 9.7:1 mixture of diastereomers and isolated as a 20:1 mixture of diastereomers as a yellow oil (313 mg, 91%). Major diastereomer: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.41 [dd, ^2J(H,H) = 10.3, $^3J_{H,H}$ = 7.3 Hz, 1 H, CH_AH_BOH], 3.52–3.66 (m, 2 H, CH$_A$$H_BOH, CH$CH=CH$_2$), 3.95 (d, J = 8.0 Hz, 1 H, Pyr–CHNH), 4.87 (d, $^3J_{H,H}$ = 17.0 Hz, 1 H, CH=CH_AH_B), 4.94 (d, $^3J_{H,H}$ = 10.1 Hz, 1 H, CH=CH$_A$$H_B$), 5.79 (ddd, J = 17.0, 10.1, 8.7 Hz, 1 H, CH=CH$_2$), 6.98–7.33 (m, 12 H, Ar-H), 8.25 ($^4J_{H,H}$ = 1.5 Hz, 1 H, pyridyl 2-H), 8.36 (dd, $^3J_{H,H}$ = 4.8, $^4J_{H,H}$ = 1.5 Hz, 1 H, pyridyl 6-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 57.2, 63.9, 64.3, 66.2, 118.0, 123.3, 127.4, 127.6, 127.8, 128.6, 128.7, 129.2, 136.2, 137.8, 138.2, 141.3, 141.4, 148.4, 150.1 ppm. HRMS (ESI): calcd. for $C_{23}H_{25}N_2O$ [M + H]$^+$ 345.1967; found 345.1974.

(2*R*)-2-{[(1*R*,2*R*)-1-(2-Furyl)-2-[(*tert*-butyldimethylsilyloxy)methyl]-but-3-en-1-yl]amino}-2-phenylethanol (1c): Obtained as a 10.7:1 mixture of diastereomers and isolated in diastereomerically pure form as an orange oil (301 mg, 75%). $[a]_D^{20}$ = –6.4 (c = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = –0.07 (s, 3 H, CH_3SiCH$_3$), 0.00 (s, 3 H, CH$_3$SiCH_3), 0.85 [s, 9 H, (CH$_3$)$_3$C], 1.94 (br. s, 1 H, NH), 2.64 (m, 1 H, CHCH=CH$_2$), 2.97 (br. s, 1 H, OH), 3.45 (dd, $^3J_{H,H}$ = 10.0, 6.7 Hz, 1 H, NHCHCH$_2$OH), 3.51 (dd, $^2J_{H,H}$ = 11.7, $^3J_{H,H}$ = 7.5 Hz, 1 H, CH_ACH$_B$OH), 3.66–3.76 (m, 3 H, CH$_A$CH_BOH, CH$_2$OSi), 4.03 (d, J = 6.2 Hz, 1 H, FurCHNH), 5.02–5.12 (m, 2 H, CH=CH_2), 5.64 (dt, J = 17.2, 10.0 Hz, 1 H, CH=CH$_2$), 6.01 (d, $^3J_{H,H}$ = 3.0 Hz, 1 H, furyl 3-H), 6.17 (dd, $^3J_{H,H}$ = 3.0, 2.0 Hz, 1 H, furyl 4-H), 7.14–7.25 (m, 6 H, Ar-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.5, –5.4, 18.2, 25.8, 50.6, 53.9, 61.4, 63.7, 65.5, 107.7, 109.6, 117.9, 127.1, 127.2, 128.3, 136.0, 141.3, 141.4, 154.7 ppm. HRMS (ESI): calcd. for $C_{23}H_{36}NO_3Si$ [M + H]$^+$ 402.2464; found 402.2466.

(2*R*)-2-{[(1*R*,2*R*)-2-[(*tert*-Butyldimethylsilyloxy)methyl]-1-phenyl-but-3-en-1-yl]amino}-2-phenylethanol (1d): Obtained as an 9.2:1 mixture of diastereomers and isolated in pure diastereomerically pure form as a pale-yellow oil (349 mg, 85%). $[a]_D^{20}$ = –23.3 (c = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.00 (s, 6 H, CH_3SiCH_3), 0.85 [s, 9 H, (CH$_3$)$_3$C], 2.60 (m, 1 H, CHCH=CH$_2$), 2.99 (br. s, 1 H, OH), 3.36 (dd, J = 9.7, 7.2 Hz, 1 H), 3.49 (dd, J = 11.5, 7.5 Hz, 1 H), 3.61 (dd, J = 10.0, 4.7 Hz, 1 H), 3.73 (m, 2 H), 4.04 (d, J = 5.0 Hz, 1 H, CH–CH–CH=CH$_2$), 5.05 (d, J = 9.7 Hz, 1 H, CH=CH_AH_B), 5.07 (d, J = 17.5 Hz, 1 H, CH=CH$_A$$H_B$), 5.52 (dt, J = 17.5, 9.7 Hz, 1 H, CH=CH$_2$), 7.14–7.23 (m, 10 H, Ar-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.5, –5.4, 18.1, 25.8, 51.1, 59.4, 60.6, 63.6, 65.0, 117.8, 126.9, 127.1, 127.3, 127.8, 128.0, 128.4, 136.0, 140.9, 141.7 ppm. HRMS (ESI): calcd. for $C_{25}H_{38}NO_2Si$ [M + H]$^+$ 412.2672; found 412.2674.

General Procedure for the Preparation of Homoallylic Amines (Method B): Small pieces of In (113 mg, 1 mmol) were added to a solution of imine (or oxazolidine) (1 mmol) and allyl bromide (1.2 mmol) in MeOH (5 mL) at room temp. The reaction mixture was stirred at room temp. for 6 h and then a saturated aqueous solution of $NaHCO_3$ (5 mL) was added. The resulting mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was dissolved in AcOEt (30 mL), washed with H_2O (10 mL), dried with $MgSO_4$, filtered and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with a mixture of PE/AcOEt (9:1) to give the corresponding amine.

(*R*)-2-[(3*S*,4*S*,*E*)-4-(Benzyloxymethyl)-1-phenylhexa-1,5-dien-3-yl-amino]-2-phenylethanol (1e): Obtained as a 14:1 mixture of diastereomers and isolated in pure diastereomerically pure form as a yellow oil (264 mg, 64%). $[a]_D^{20}$ = –13.2 (c = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.75 (m, 1 H, CH–CH=CH$_2$), 3.41–3.58 (m, 4 H, CH_AH$_B$OH, CH_2OBn, Ph–CH=CH–CHNH), 3.69 (dd, $^2J_{H,H}$ = 10.6, $^3J_{H,H}$ = 4.5 Hz, 1 H, CH$_A$$H_B$OH), 3.86 (dd, $^3J_{H,H}$ = 7.1, 4.6 Hz, 1 H, NHCH–CH$_2$OH), 4.42 (d, $^2J_{H,H}$ = 12.0 Hz, 1 H, CH_AH$_B$Ph), 4.50 (d, $^2J_{H,H}$ = 12.0 Hz, 1 H, CH$_A$$H_B$Ph), 5.17–5.26 (m, 2 H, CH=CH_2), 5.74 (m, 1 H, CH=CH$_2$), 5.83 (dd, $^3J_{H,H}$ = 15.8, 8.7 Hz, 1 H, Ph–CH=CH), 6.33 (d, $^3J_{H,H}$ = 15.8 Hz, 1 H, Ph–CH=CH), 7.13–7.28 (m, 15 H, Ar-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 48.2, 59.0, 61.1, 65.8, 70.9, 72.9, 118.4, 126.2, 127.2, 127.25, 127.4, 1247.5, 127.7, 128.2, 128.3, 128.4, 129.8, 131.7, 135.6, 136.7, 138.1, 141.8 ppm.

(*R*)-2-[(3*S*,4*S*,*E*)-4-[(*tert*-Butyldimethylsilyloxy)methyl]-1-phenylhexa-1,5-dien-3-ylamino]-2-phenylethanol (1f): Obtained as a 13:1 mixture of diastereomers and isolated in pure diastereomerically pure form as a yellow oil (363 mg, 83%). $[a]_D^{20}$ = +1.2 (c = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.00 [s, 6 H, (CH$_3$)$_2$Si], 0.84 [s, 9 H, (CH$_3$)$_3$C], 2.58 (m, 1 H, CH–CH=CH$_2$), 3.46–3.71 (m, 5 H, CH$_2$OSi, NHCHCH_2OH), 3.87 (dd, $^3J_{H,H}$ = 7.1, 4.5 Hz, 1 H, Ph–CH=CH–CH), 5.13–5.23 (m, 2 H, CH=CH_2), 5.68 (dt, $^3J_{H,H}$ = 17.3, 8.7 Hz, 1 H, CH=CH$_2$), 5.87 (dd, $^3J_{H,H}$ = 15.8, 8.7 Hz, 1 H, Ph–CH=CH), 6.38 (d, $^3J_{H,H}$ = 15.8 Hz, 1 H, Ph–CH=CH), 7.14–7.25 (m, 10 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.5, –5.4, 18.1, 25.8, 50.4, 58.2, 61.1, 63.6, 65.9, 118.3, 126.1, 127.2 (3 C), 128.30, 128.35, 129.7, 131.7, 135.6, 136.8, 141.8 ppm. HRMS (ESI): calcd. for $C_{27}H_{40}NO_2Si$ [M + H]$^+$ 438.2828; found 438.2820.

(*R*)-2-[(2*R*,3*R*)-1-Benzyloxy-3-phenylpent-4-en-2-ylamino]-2-phenylethanol (1g): Obtained as a 2:1 mixture of diastereomers and isolated in pure diastereomerically pure form as a yellow oil (143 mg, 37%). $[a]_D^{20}$ = –47.7 (c = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.10 (br. s, 2 H, NH, OH), 2.98 (m, 1 H, CH–CH=CH$_2$), 3.17–3.26 (m, 2 H, CH_2OBn), 3.43 (m, 2 H), 3.53–3.63 (m, 2 H), 4.21 (s, 2 H, OCH_2Ph), 5.06–5.16 (m, 2 H, CH=CH_2), 6.05 (dt, $^3J_{H,H}$ = 16.7, 9.7 Hz, 1 H CH=CH$_2$), 7.16–7.34 (m, 15 Ar-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 52.8, 60.2, 63.4, 66.5, 69.7, 72.9, 116.8, 126.4, 126.9, 127.3, 127.50, 127.55, 128.0, 128.2, 128.4, 128.5, 138.1, 138.4, 141.6, 142.5 ppm. HRMS (ESI): calcd. for $C_{26}H_{30}NO_2$ [M + H]$^+$ 388.2277; found 388.2274.

(*R*)-2-[(2*R*,3*S*)-1-Benzyloxy-3-vinyloctan-2-ylamino]-2-phenylethanol (1h): Obtained as a 5:1 mixture of diastereomers and isolated in pure diastereomerically pure form as a yellow oil (282, 74%). $[a]_D^{20}$ = –40.2 (c = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.85 (t, $^3J_{H,H}$ = 6.4 Hz, 3 H CH$_3$), 1.08–1.43 [m, 8 H CH$_3$-(CH_2)$_4$], 1.99 (br. s, 1 H, NH), 2.28 (app. sept, $^3J_{H,H}$ = 4.3 Hz, 1 H, CH–CH=CH$_2$), 2.73 (dt, J = 6.7, 4.3 Hz, 1 H, BnOCH$_2$CHNH), 3.18 (br. s, 1 H, OH), 3.32–3.44 (m, 3 H, CH_2OBn, CH$_A$$H_B$OH), 3.64 (dd, $^2J_{H,H}$ = 10.5, $^3J_{H,H}$ = 4.5 Hz, 1 H, CH$_A$$H_B$OH), 3.88 (dd, $^3J_{H,H}$ = 9.2, 4.5 Hz, 1 H, CH–CH$_2$OH), 4.32 (s, 2 H, OCH_2Ph), 5.02–5.11 (m, 2 H, CH=CH_2), 5.62 (dt, $^3J_{H,H}$ = 16.5, 10.5 Hz, 1 H, CH=CH$_2$), 7.23–7.36 (m, 10 Ar-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 14.0, 22.5, 27.3, 30.9, 31.8, 45.3, 57.8, 61.7, 66.8, 70.2, 72.8, 116.6, 126.9, 127.0, 127.2, 127.4, 128.3, 128.5, 128.2, 139.2, 141.2 ppm. HRMS (ESI): calcd. for $C_{25}H_{36}NO_2$ [M + H]$^+$ 382.2746; found 382.2737.

(*R*)-2-[(3*S*,4*S*)-3-(Benzyloxymethyl)-5-methylhept-1-en-4-ylamino]-2-phenylethanol (1i): Obtained as a 11:1 mixture of diastereomers

and isolated in pure diastereomerically pure form as a pale-yellow oil (198 mg, 54%). $[\alpha]_D^{20}$ = –104.9 (*c* = 1, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.46 (d, $^3J_{H,H}$ = 6.5 Hz, 3 H, C*H*$_3$–CH–CH_3), 0.81 (d, $^3J_{H,H}$ = 6.8 Hz, 3 H, CH_3–CH–CH_3), 0.97–1.18 (m, 2 H, CH_2-*i*Pr), 1.58 (m, 1 H, CH_3–CH–CH_3), 2.67–2.82 (m, 2 H, C*H*–CH=CH_2, C*H*–CH_2-*i*Pr), 3.37 (dd, *J* = 9.0, 6.8 Hz, 1 H, CH_AH_BOBn), 3.47–3.53 (m, 2 H, CH_AH_BOBn, CH_AH_BOH), 3.65 (dd, *J* = 10.5, 4.7 Hz, 1 H, CH_AH_BOH), 3.89 (dd, *J* = 8.5, 4.7 Hz, 1 H, NHC*H*Ph), 4.41 (d, *J* = 12.0 Hz, 1 H, CH_AH_BPh), 4.47 (d, *J* = 12.0 Hz, 1 H, CH_AH_BPh), 5.17–5.23 (m, 2 H, CH=CH_2), 5.77 (m, 1 H, C*H*=CH_2), 7.21–7.34 (m, 10 H, Ar-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 21.1, 24.0, 24.3, 40.5, 45.6, 52.1, 61.3, 66.8, 71.1, 72.8, 127.4, 127.5, 127.6, 128.2, 128.4, 136.4, 138.3, 141.1 ppm. HRMS (ESI): calcd. for $C_{24}H_{34}NO_2$ $[M + H]^+$ 368.2590; found 368.2592.

(*R*)-2-{(3*S*,4*S*)-7-Benzyloxy-3-[(*tert*-butyldimethylsilyloxy)methyl]-hept-1-en-4-ylamino}-2-phenylethanol (1j): Obtained as a 10:1 mixture of diastereomers and isolated in pure diastereomerically pure form as a pale-yellow oil (237 mg, 49%). $[\alpha]_D^{20}$ = –50.8 (*c* = 1, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.00 (s, 3 H, C*H*$_3$SiCH$_3$), 0.01 (s, 3 H, CH$_3$SiC*H*$_3$), 0.83 [s, 9 H, $(CH_3)_3$Si], 1.14–1.80 [m, 5 H, CH-(CH_2)$_2$–CH_2OSi, NH], 2.52–2.72 (m, 2 H, NHC*H*–CH–CH=CH_2), 3.31 (t, $^3J_{H,H}$ = 6.4 Hz, 2 H, CH_2-OBn), 3.49–3.58 (m, 2 H, CH_2O), 3.64–3.73 (m, 2 H, CH_2O), 3.90 (dd, $^3J_{H,H}$ = 8.5, 4.5 Hz, 1 H, NHC*H*–CH_2OH), 4.44 (s, 2 H, OCH_2Ph), 5.15–5.22 (m, 2 H, CH=CH_2), 5.73 (m, 1 H, C*H*=CH_2), 7.30–7.36 (m, 10 Ar-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.0, –4.9, 18.6, 26.3, 26.9, 27.6, 48.8, 54.3, 61.9, 6.4, 67.6, 70.9, 73.2, 118.3, 127.9, 128.1 (3 C), 128.8, 128.9, 136.9, 139.0, 141.8 ppm.

(*R*)-2-{(3*S*,4*S*)-3-(Benzyloxymethyl)-7-[(*tert*-butyldimethylsilyloxy)methyl]hept-1-en-4-ylamino}-2-phenylethanol (1k): Obtained as a 9:1 mixture of diastereomers and isolated in pure diastereomerically pure form as a pale-yellow oil (362 mg, 75%). $[\alpha]_D$ = –87.5 (*c* = 1, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.00 (s, 3 H, C*H*$_3$SiCH$_3$), 0.01 (s, 3 H, CH$_3$SiC*H*$_3$), 0.88 [s, 9 H, $(CH_3)_3$Si], 1.10–1.63 [m, 4 H, CH-(CH_2)$_2$–CH_2OBn], 2.61–2.76 (m, 2 H, NHC*H*–CH–CH=CH_2), 3.39–3.67 (m, 6 H, CH_2OH, CH_2OSi, CH_2OBn), 3.88 (dd, $^3J_{H,H}$ = 8.4, 4.4 Hz, 1 H, NHC*H*–CH_2OH), 4.43 (d, $^2J_{H,H}$ = 12.1 Hz, 1 H), 4.49 (d, $^2J_{H,H}$ = 11.1 Hz, 1 H), 5.17–5.23 (m, 2 H, CH=CH_2), 5.79 (m, 1 H, C*H*=CH_2), 7.25–7.35 (m, 10 H, Ar-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.4, 18.2, 25.9, 27.2, 29.2, 46.1, 54.7, 61.6, 62.9, 66.9, 71.3, 72.8, 117.6, 126.8, 127.4, 127.5, 128.2, 128.4, 136.7, 138.2, 141.2 ppm.

(2*R*)-2-{[(1*S*,2*S*)-2-[(*tert*-Butyldimethylsilyloxy)methyl]-1-hexylbut-3-en-1-yl]amino}-2-phenylethanol (1l): Obtained as a 17:1 mixture of diastereomers and isolated in pure diastereomerically pure form as a colourless oil (293 mg, 70%). $[\alpha]_D^{20}$ = –83.2 (*c* = 1, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = –0.01 (C*H*$_3$SiCH$_3$), 0.00 (s, 3 H, CH$_3$SiC*H*$_3$), 0.82 [m, 12 H, $(CH_3)_3$Si, CH_3–CH_2], 1.07–1.34 [m, 11 H, CH_3-(CH_2)$_5$–CH, NH], 2.51–2.73 (m, 3 H, NHC*H*–CH, OH), 3.48–3.56 (m, 2 H, CH_2-O), 3.63–3.71 (m, 2 H, CH_2-O), 3.86 (dd, $^3J_{H,H}$ = 8.5, 4.5 Hz, 1 H, NHC*H*–CH_2OH), 5.11–5.18 (m, 2 H, CH=CH_2), 5.72 (m, 1 H, C*H*=CH_2), 7.28–7.30 (m, 5 H, Ar-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.5, –5.4, 14.0, 18.2, 22.6, 25.8, 26.0, 29.2, 30.5, 31.8, 48.4, 53.8, 61.5, 63.8, 66.9, 117.5, 127.4, 127.5, 128.4, 136.6, 141.4 ppm. HRMS (ESI): calcd. for $C_{25}H_{46}NO_2Si$ $[M + H]^+$ 420.3298; found 420.3305.

(2*R*)-2-{[(1*S*,2*S*)-2-[(*tert*-Butyldimethylsilyloxy)methyl]-1-methylbut-3-en-1-yl]amino}-2-phenylethanol (1m): Obtained as a 7.6:1 mixture of diastereomers and isolated as an 11:1 mixture of diastereomers in pure form as a colourless oil (179 mg, 55%). $[\alpha]_D^{20}$ = –71.3 (*c* = 1, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.90 (d, $^3J_{H,H}$ = 6.5 Hz, 3 H, CH_3), 2.20 (br. s, 1 H, NH), 2.61 (m, 1 H, C*H*–CH=CH_2), 2.86 (m, 1 H, C*H*–CH_3), 3.38–3.57 (m, 3 H, CH_2OBn, CH_AH_BOH), 3.64 (dd, $^2J_{H,H}$ = 10.7, $^3J_{H,H}$ = 4.5 Hz, 1 H, CH_AH_BOH), 3.88 (dd, $^3J_{H,H}$ = 8.2, 4.2 Hz, 1 H, PhC*H*NH), 4.44 (d, $^2J_{H,H}$ = 12.2 Hz, 1 H, PhCH_AH_BO), 4.48 (d, $^2J_{H,H}$ = 12.2 Hz, 1 H, PhCH_AH_BO), 5.17–5.28 (m, 2 H, CH=CH_2), 5.77 (m, 1 H, C*H*=CH_2), 7.26–7.34 (m, 10 H, Ar-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 17.9, 47.6, 50.7, 61.7, 66.8, 71.3, 72.9, 117.9, 127.1, 127.40, 127.45, 127.50, 128.2, 128.5, 136.2, 138, 2, 141.5 ppm. HRMS (ESI): calcd. for $C_{21}H_{28}NO_2$ $[M + H]^+$ 326.2120; found 326.2133.

***tert*-Butyl Benzyl{(4*S*,5*S*)-5-(benzyloxymethyl)-4-[(*R*)-2-hydroxy-1-phenylethylamino]hept-6-enyl}carbamate (1n):** Obtained as a 3:1 mixture of diastereomers and isolated in pure diastereomerically pure form as a pale-orange oil (163 mg, 30%). $[\alpha]_D^{20}$ = –38.3 (*c* = 1, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = 1.41 [br. s, 9 H, $(CH_3)_3$C], 1.52 (br. m, 2 H), 1.86 (br. s, 1 H, NH), 2.40–3.00 (br. m, 4 H), 3.10–3.64 (br. m, 4 H), 3.60 (dd, $^2J_{H,H}$ = 10.6, $^3J_{H,H}$ = 4.3 Hz, 1 H, CH_AH_BOH), 3.85 (br. s, 1 H, NHC*H*CH_2OH), 4.15–4.30 (br. m, 2 H, PhCH_2N), 4.38 (d, $^2J_{H,H}$ = 12.6 Hz, 1 H, CH_AH_BOBn), 4.43 (d, $^2J_{H,H}$ = 12.6 Hz, 1 H, CH_AH_BOBn), 5.13–5.21 (m, 2 H, CH=CH_2), 5.69 (m, 1 H, C*H*=CH_2) 7.10–7.35 (m, 15 H, Ar-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 28.4, 29.9 (br.), 44.6, 45.5, 50.3 (br), 52.9, 61.5, 67.2, 71.2, 72.8, 79.5, 118.1, 127.0, 127.40, 127.45, 127.6, 128.2, 128.3, 128.4, 136.1, 138.4 (br), 141.0, 155.6 ppm. HRMS (ESI): calcd. for $C_{34}H_{45}N_2O_4$ $[M + H]^+$ 545.3379; found 545.3381.

General Procedure for the Preparation of Pyrrolidines 2 (Method C): $Cp_2Zr(H)Cl$ (772 mg, 3 mmol) was added in one portion to a solution of homoallylic amine **1** (1 mmol) in CH_2Cl_2 (3 mL) under argon and the resulting mixture was stirred until complete dissolution. Then I_2 (254 mg, 1 mmol) was added and the reaction mixture was stirred for 2 h. CH_2Cl_2 (10 mL) was added and the organic phase was washed with HCl (1 M, 2 × 3 mL) and Na_2CO_3 (10%, 2 × 3 mL), dried with $MgSO_4$, filtered and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with a mixture of PE/AcOEt to give the corresponding pyrrolidine **2**.

(2*R*)-2-[(2*R*,3*R*)-2-(2-Furyl)-3-phenylpyrrolidin-1-yl]-2-phenylethanol (2a): Pale-yellow oil (250 mg, 75%). $[\alpha]_D^{20}$ = –35.6 (*c* = 1, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = 2.03–2.54 (m, 3 H, 4-H, 4-H pyrrolidine, OH), 3.03 (m, 1 H, 5-H pyrrolidine), 3.19 (m, 1 H, 5′-H pyrrolidine), 3.43 (m, 1 H, 3-H pyrrolidine), 3.70–3.82 (m, 3 H, NC*H*Ph–CH_2OH), 4.38 (d, *J* = 7.9 Hz, 1 H, 2-H pyrrolidine), 5.84 (m, 1 H, 3-H furyl), 6.10 (m, 1 H, 4-H furyl), 6.91–7.37 (m, 11 H, 5-H furyl, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 28.9, 49.9, 51.5, 61.5, 64.0, 67.4, 108.5, 110.3, 126.6, 128.1, 128.4, 128.7, 129.2, 138.7, 139.9, 141.7, 155.4 ppm. HRMS (ESI): calcd. for $C_{22}H_{24}NO_2$ $[M + H]^+$ 334.1807; found 334.1822.

(2*R*)-2-[(2*R*,3*R*)-3-[(*tert*-Butyldimethylsilyloxy)methyl]-2-(2-furyl)-pyrrolidin-1-yl]-2-phenylethanol (2c): Yellow oil (301 mg, 75%). $[\alpha]_D^{20}$ = –6.1 (*c* = 1, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = –0.02 (s, 3 H, C*H*$_3$SiCH$_3$), 0.00 (s, 3 H, CH$_3$SiC*H*$_3$), 0.91 [s, 9 H, $(CH_3)_3$-C], 1.79 (tt, $^2J_{H,H}$ = 12.1, $^3J_{H,H}$ = 8.7 Hz, 1 H, 4-H pyrrolidine), 2.03 (m, 1 H, 4′-H pyrrolidine), 2.43 (br. s, 1 H, OH), 2.54 (dt, $^3J_{H,H}$ = 11.0, 7.5 Hz, 1 H, 3-H pyrrolidine), 2.93 (q, $^3J_{H,H}$ = 8.0 Hz, 1 H, 5-H pyrrolidine), 3.07 (td, $^3J_{H,H}$ = 8.7, 3.0 Hz, 1 H, 5′-H pyrrolidine), 3.29 (dd, $^2J_{H,H}$ = 10.1, $^3J_{H,H}$ = 2.5 Hz, 1 H, CH_AH_BOSi), 3.32 (dd, $^2J_{H,H}$ = 10.1, $^3J_{H,H}$ = 2.7 Hz, 1 H, CH_AH_BOSi), 3.76 (m, 3 H, NC*H*–CH_2OH), 4.29 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, 2-H pyrrolidine), 6.16 (d, *J* = 3.0 Hz, 1 H, 3-H furyl), 6.39 (dd, $^3J_{H,H}$ = 3.0, 2.0 Hz, 1 H, 4-H furyl), 7.28–7.42 (m, 6 H,

5-H furyl, Ph-H) ppm. ^{13}C NMR: δ = –5.6, –5.5, 25.8, 46.1, 50.7, 57.7, 63.5, 63.6, 66.6, 108.0, 110.0, 127.5, 128.2, 128.7, 138.4, 141.5, 155.2 ppm.

(2*R*)-2-[(2*R*,3*R*)-2-(Benzyloxymethyl)-3-phenylpyrrolidin-1-yl]-2-phenylethanol (2g): Pale-yellow oil (298 mg, 77%). $[\alpha]_D^{20}$ = +4.2 (*c* = 1, CH_2Cl_2). ^{1}H NMR: δ = 1.92 (m, 1 H, 4-H pyrrolidine), 2.21 (m, 1 H, 4′-H pyrrolidine), 2.88 (dt, $^2J_{H,H}$ = 12.0, $^3J_{H,H}$ = 7.4 Hz, 1 H, 5-H pyrrolidine), 2.95–3.12 (m, 3 H, C*H*$_2$OBn, 2-H pyrrolidine), 3.29 (t, $^3J_{H,H}$ = 7.9 Hz, 1 H, 5′-H pyrrolidine), 3.59 (m, 1 H, 3-H pyrrolidine), 3.73 (dd, $^2J_{H,H}$ = 10.1, $^3J_{H,H}$ = 4.0 Hz, 1 H, C*H*$_A$H$_B$OH), 3.90–4.06 (m, 2 H, NC*H*–CH$_A$*H*$_B$OH), 4.22 (s, 2 H, C*H*$_2$OBn), 7.10–7.36 (m, 15 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 28.4, 46.8, 51.1, 60.5, 63.2, 67.6, 67.6, 71.6, 73.2, 126.2, 127.5, 127.6, 128.10, 128.15, 128.20, 128.4, 128.7, 137.8, 138.5, 139.9 ppm. HRMS (ESI): calcd. for $C_{26}H_{30}NO_2$ [M + H]$^+$ 388.2277; found 388.2280.

(2*R*)-2-[(2*R*,3*S*)-2-(Benzyloxymethyl)-3-pentylpyrrolidin-1-yl]-2-phenylethanol (2h): Pale-yellow oil (255 mg, 67%). $[\alpha]_D^{20}$ = –7.0 (*c* = 0.2, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.84 (t, $^3J_{H,H}$ = 6.4 Hz, 3 H, CH_3), 1.08–1.34 [m, 8 H, $(CH_2)_4$], 1.39–1.60 (m, 2 H, 4-H pyrrolidine), 1.74 (m, 1 H, 3-H pyrrolidine), 2.79 (td, $J_{H,H}$ = 9.0, 6.7 Hz, 1 H, 5′-H pyrrolidine), 3.11 (t, $^3J_{H,H}$ = 7.6 Hz, 1 H, 5′-H pyrrolidine), 3.23–3.39 (m, 3 H, C*H*$_2$OBn, 2-H pyrrolidine), 3.55 (dd, $^2J_{H,H}$ = 10.5, $^3J_{H,H}$ = 4.5 Hz, 1 H, C*H*$_A$H$_B$OH), 3.84 (dd, $^3J_{H,H}$ = 8.5, 4.5 Hz, 1 H, NC*H*–CH$_2$OH), 3.97 (dd, $^2J_{H,H}$ = 10.2, $^3J_{H,H}$ = 8.8 Hz, 1 H, CH$_A$*H*$_B$OH), 4.45 (d, $^2J_{H,H}$ = 12.2 Hz, 1 H, OC*H*$_A$H$_B$Ph), 4.46 (d, $^2J_{H,H}$ = 12.2 Hz, 1 H, OCH$_A$*H*$_B$Ph), 7.30–7.39 (m, 10 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 14.0, 22.5, 28.4, 29.6, 30.4, 32.0, 41.9, 51.2, 58.6, 63.4, 67.9, 71.2, 73.3, 127.50, 127.55, 127.7, 128.2, 128.3, 128.7, 138.0, 138.9 ppm.

(2*R*)-2-[(2*S*,3*S*)-3-(Benzyloxymethyl)-2-isobutylpyrrolidin-1-yl]-2-phenylethanol (2i): Isolated in pure diastereomerically pure form as a pale-yellow oil (71%) starting from a 25:1 mixture of diastereomers. $[\alpha]_D^{20}$ = –4.0 (*c* = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.73 (d, $^3J_{H,H}$ = 6.5 Hz, 3 H, C*H*$_3$–CH–CH$_3$), 0.74 (d, $^3J_{H,H}$ = 6.3 Hz, 3 H, CH$_3$–CH–CH$_3$), 1.09 (t, $^3J_{H,H}$ = 6.5 Hz, 2 H, C*H*$_2$-*i*Pr), 1.48–1.60 (m, 2 H, 4-H pyrrolidine), 1.85 (m, 1 H, CH$_3$–CH–CH$_3$), 2.19 (hex., $^3J_{H,H}$ = 7.5 Hz, 1 H, 3-H pyrrolidine), 2.74–2.85 (m, 2 H, 5-H pyrrolidine, OH), 2.93–3.02 (m, 2 H, 2-H pyrrolidine, 5′-H pyrrolidine), 3.34 (dd, $^2J_{H,H}$ = 9.0, $^3J_{H,H}$ = 7.5 Hz, 1 H, C*H*$_A$H$_B$OBn), 3.42 (dd, $^2J_{H,H}$ = 9.0, $^3J_{H,H}$ = 7.3 Hz, 1 H, CH$_A$*H*$_B$OBn), 3.69–3.88 (m, 3 H, NC*H*–CH$_2$OH), 4.42 (s, 2 H, PhC*H*$_2$O), 7.21–7.32 (m, 10 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 22.6, 23.2, 24.8, 26.9, 38.5, 41.2, 49.9, 58.8, 63.2, 67.2, 70.4, 72.9, 127.4, 127.50, 127.55, 128.20, 128.25, 128.7, 138.2, 139.6 ppm. HRMS (ESI): calcd. for $C_{24}H_{34}NO_2$ [M + H]$^+$ 368.2590; found 368.2585.

(2*R*)-2-{(2*S*,3*S*)-2-[3-(Benzyloxy)propyl]-3-[(*tert*-butyldimethylsilyloxy)methyl]pyrrolidin-1-yl}-2-phenylethanol (2j): Pale-yellow oil (227 mg, 47%). $[\alpha]_D^{20}$ = –8.5 (*c* = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.00 [s, 6 H, $(CH_3)_2$Si], 0.86 [s, 9 H, $(CH_3)_3$C], 1.24–1.66 [m, 5 H, OCH$_2$-(C*H*$_2$)$_2$, 4-H pyrrolidine], 1.81 (m, 1 H, 4-H pyrrolidine), 2.03 (m, 1 H, 3-H pyrrolidine), 2.69 (br. s, 1 H, OH), 2.82 (dt, $^2J_{H,H}$ = 9.7, $^3J_{H,H}$ = 7.9 Hz, 1 H, 5-H pyrrolidine), 2.93 (q, $^3J_{H,H}$ = 6.3 Hz, 1 H, 2-H pyrrolidine), 3.02 (td, $^2J_{H,H}$ = 9.7, $^3J_{H,H}$ = 6.0 Hz, 1 H, 5′-H pyrrolidine), 3.37 [t, $^3J_{H,H}$ = 6.5 Hz, 2 H, OC*H*$_2$-(CH$_2$)$_2$], 3.52 (dd, $^2J_{H,H}$ = 9.9, $^3J_{H,H}$ = 7.5 Hz, 1 H, C*H*$_A$H$_B$OSi), 3.61 (dd, $^2J_{H,H}$ = 10.1, $^3J_{H,H}$ = 7.4 Hz, 1 H, CH$_A$*H*$_B$OSi), 3.74 (t, $^3J_{H,H}$ = 6.1 Hz, 1 H, NC*H*–CH$_2$OH), 3.81–3.90 (m, 2 H, C*H*$_2$OH), 4.47 (s, 2 H, PhC*H*$_2$O), 7.28–7.34 (m, 10 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.4, 18.1, 25.8, 25.9, 26.7, 27.1, 44.1, 50.3, 60.6, 62.9, 63.4, 67.6, 70.6, 72.7, 127.5, 128.2, 128.7, 138.6, 139.6 ppm.

(2*R*)-2-{(2*S*,3*S*)-3-(Benzyloxymethyl)-2-[3-(*tert*-butyldimethylsilyloxy)propyl]pyrrolidin-1-yl}-2-phenylethanol (2k): Pale-yellow oil (309 mg, 64%). $[\alpha]_D^{20}$ = –3.7 (*c* = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.05 [s, 6 H, $(CH_3)_2$Si], 0.91 [s, 9 H, $(CH_3)_3$C], 1.16–1.63 [m, 5 H, OCH$_2$-(C*H*$_2$)$_2$, 4-H pyrrolidine], 1.88 (m, 1 H, 4′-H pyrrolidine), 2.26 (m, 1 H, 3-H pyrrolidine), 2.60 (br. s, 1 H, OH), 2.81 (dt, *J* = 9.6, 7.9 Hz, 1 H, 5-H pyrrolidine), 2.93–3.13 (m, 2 H, 2-H, 5′-H pyrrolidine), 3.39 (dd, $^2J_{H,H}$ = 9.0, $^3J_{H,H}$ = 7.3 Hz, 1 H, C*H*$_A$H$_B$OSi), 3.46–3.53 [m, 4 H, OC*H*$_2$-(CH$_2$)$_2$, C*H*$_2$OBn], 3.72–3.91 (m, 3 H, NC*H*–C*H*$_2$OH), 4.42 (d, $^2J_{H,H}$ = 12.1 Hz, 1 H, PhC*H*$_A$H$_B$O), 4.48 (d, $^2J_{H,H}$ = 12.1 Hz, 1 H, PhCH$_A$*H*$_B$O), 7.28–7.33 (m, 10 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.8, 25.2, 25.5, 26.7, 29.7, 41.0, 49.8, 60.3, 62.8, 63.1, 67.1, 70.0, 72.5, 127.0, 127.10, 127.15, 127.80, 127.85, 128.2 ppm (quaternary C atoms are missing).

(2*R*)-2-[(2*S*,3*S*)-2-[(*tert*-Butyldimethylsilyloxy)methyl]-2-hexylpyrrolidin-1-yl]-2-phenylethanol (2l): Colourless oil (264 mg, 63%). $[\alpha]_D^{20}$ = –5.3 (*c* = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.00 [s, 6 H, $(CH_3)_2$Si], 0.85–0.87 [m, 12 H, C*H*$_3$–CH$_2$, $(CH_3)_3$C], 1.18–1.27 [m, 10 H, (C*H*$_2$)$_5$], 1.50 (m, 1 H, 4-H pyrrolidine), 1.79 (dtd, *J* = 12.2, 8.1, 3.9 Hz, 1 H, 4′-H pyrrolidine), 2.01 (sext, *J* = 7.7 Hz, 1 H, 3-H pyrrolidine), 2.82 (q, $^3J_{H,H}$ = 8.1 Hz, 1 H, 5-H pyrrolidine), 2.89 (m, 1 H, 2-H pyrrolidine), 3.03 (m, 1 H, 5-H pyrrolidine), 3.49 (dd, $^2J_{H,H}$ = 10.2, $^3J_{H,H}$ = 7.5 Hz, 1 H, C*H*$_A$H$_B$OSi), 3.59 (dd, $^2J_{H,H}$ = 10.2, $^3J_{H,H}$ = 7.2 Hz, 1 H, CH$_A$*H*$_B$OSi), 3.75 (t, $^3J_{H,H}$ = 6.5 Hz, 1 H, NC*H*Ph), 3.80 (dd, $^2J_{H,H}$ = 10.4, $^3J_{H,H}$ = 6.5 Hz, 1 H, C*H*$_A$H$_B$OH), 3.87 (dd, $^2J_{H,H}$ = 10.4, $^3J_{H,H}$ = 6.5 Hz, 1 H, CH$_A$*H*$_B$OH), 7.29–7.33 (m, 5 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.2, 14.2, 18.3, 22.8, 26.0, 26.8, 27.1, 29.5, 29.9, 32.0, 44.3, 50.6, 61.0, 63.1, 63.5, 67.7, 127.7, 128.5, 128.9, 139.7 ppm. HRMS (ESI): calcd. for $C_{25}H_{46}NO_2Si$ [M + H]$^+$ 420.3298; found 420.3302.

(2*R*)-2-[(2*S*,3*S*)-3-(Benzyloxymethyl)-2-methylpyrrolidin-1-yl]-2-phenylethanol (2m): Isolated as a 13:1 mixture of diastereomers in pure diastereomerically pure form starting from a 9:1 mixture of diastereomers as a pale-yellow oil (208 mg, 64%). Major diastereomer: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.00 (d, $^3J_{H,H}$ = 6.8 Hz, 3 H, CH_3), 1.59 (m, 1 H, 4-H pyrrolidine), 1.92 (m, 1 H, 4′-H pyrrolidine), 2.50 (m, 1 H, 3-H pyrrolidine), 2.96 (dd, $^2J_{H,H}$ = 12.7, $^3J_{H,H}$ = 8.0 Hz, 1 H), 3.20 (m, 1 H, 5-H pyrrolidine), 3.35–3.57 (m, 3 H, C*H*$_2$OBn, 2-H pyrrolidine), 3.90 (q, $^3J_{H,H}$ = 8.6 Hz, 1 H, C*H*–CH$_2$OH), 4.05 (m, 2 H, C*H*$_2$OH), 4.44 (br. s, 1 H, OH), 4.46 (s, 2 H, PhC*H*$_2$O), 7.20–7.36 (m, 10 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 12.8, 25.7, 41.5, 51.1, 58.5, 63.0, 68.0, 69.9, 73.2, 127.7, 127.8, 128.4, 128.5, 128.7, 129.0, 136.7, 137.8 ppm. HRMS (ESI): calcd. for $C_{21}H_{28}NO_2$ [M + H]$^+$ 326.2120; found 326.2109.

***tert*-Butyl Benzyl(3-{(2*S*,3*S*)-3-(benzyloxymethyl)-1-[(*R*)-2-hydroxy-1-phenylethyl]pyrrolidin-2-yl}propyl)carbamate (2n):** Yellow oil (316 mg, 58%). $[\alpha]_D^{20}$ = –5.3 (*c* = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.44 [m, 12 H, $(CH_3)_3$-C, 4-H pyrrolidine, NBoc–CH$_2$–CH$_2$], 1.81 (m, 1 H, 4′-H pyrrolidine), 2.20 (m, 1 H, 3-H pyrrolidine), 2.62 (br. s, 1 H, OH), 2.74 (q, *J* = 8.2 Hz, 1 H, 5-H pyrrolidine), 2.86–3.18 (m, 3 H, 2-H, 5′-H pyrrolidine), 3.30–3.50 (m, 3 H), 3.60–3.82 (m, 3 H), 4.24–4.41 (m, 4 H, NC*H*$_2$Ph, OC*H*$_2$Ph), 7.14–7.34 (m, 15 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 27.0, 27.8, 28.4, 41.4, 44.8, 49.8, 50.6, 59.0, 63.7, 67.6, 70.2, 72.9, 79.5, 126.9, 127.4, 127.5 (2 C), 128.2, 128.3 (2 C), 128.6 (2 C), 138.2, 138.6, 139.7, 155.7 ppm. HRMS (ESI): calcd. for $C_{34}H_{45}N_2O_4$ [M + H]$^+$ 545.3379; found 545.3390.

General Procedure for the Preparation of Pyrrolidines 3 (Method D): A mixture of homoallylic amine **2** (1 mmol) and $Pd(OH)_2/C$ (20%, 60 mg) in MeOH (5 mL) under hydrogen was stirred overnight at room temp. The crude mixture was filtered through a pad of Celite and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using Et_2O/Et_2NH gradient elution (100:0→98:2) to give the corresponding amine.

(2*R*,3*R*)-2-(Benzyloxymethyl)-3-phenylpyrrolidine (3g): Colourless oil (214 mg, 80%). $[\alpha]_D^{20}$ = –46 (*c* = 1, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = 2.05 (m, 1 H, 4-H pyrrolidine), 2.21 (dtd, $^2J_{H,H}$ = 16.6, $^3J_{H,H}$ = 8.2, 3.8 Hz, 1 H, 4′-H pyrrolidine), 2.35 (br. s, 1 H, NH), 2.98–3.12 (m, 3 H, 5-H pyrrolidine, CH_2OBn), 3.28 (ddd, *J* = 10.1, 8.8, 3.8 Hz, 1 H, 5′-H pyrrolidine), 3.40 (q, $^3J_{H,H}$ = 7.5 Hz, 1 H, 2-H pyrrolidine), 3.53 (td, $^3J_{H,H}$ = 7.4, 4.9 Hz, 1 H, 3-H pyrrolidine), 4.27 (s, 2 H, PhCH_2O), 7.17–7.33 (m, 10 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 31.7, 45.4, 46.2, 61.6, 71.7, 73.1, 126.1, 127.4, 127.5, 128.0, 128.2, 128.3, 138.2, 141.6 ppm. HRMS (ES+): calcd. for $C_{18}H_{22}NO$ $[M + H]^+$ 268.1701; found 268.1696.

(2*S*,3*S*)-3-(Benzyloxymethyl)-2-isobutylpyrrolidine (3i): Colourless oil (185 mg, 75%). $[\alpha]_D^{20}$ = +37.3 (*c* = 2, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.89 (d, $^3J_{H,H}$ = 6.8 Hz, 3 H, CH_3–CH–CH_3), 0.92 (d, $^3J_{H,H}$ = 6.5 Hz, 3 H, CH_3–CH–CH_3), 1.29 (m, 2 H, CH_2-*i*Pr), 1.60–1.78 (m, 3 H, 4-H, 4′-H pyrrolidine, NH), 1.94 [dtd, *J* = 12.7, 8.8, 4.8 Hz, 1 H, CH-$(CH_3)_2$], 2.27 (m, 1 H, 3-H pyrrolidine), 2.80 (ddd, *J* = 10.7, 8.7, 7.2 Hz, 1 H, 5-H pyrrolidine), 3.00–3.12 (m, 2 H, 2-H, 5′-H pyrrolidine), 3.37 (dd, $^2J_{H,H}$ = 9.0, $^3J_{H,H}$ = 6.7 Hz, 1 H, C$H_A$$H_B$OSi), 3.47 (dd, $^2J_{H,H}$ = 9.0, $^3J_{H,H}$ = 6.0 Hz, 1 H, $CH_A$$H_B$OSi), 4.48 (s, 2 H, PhC$H_2$O), 7.33 (m, 5 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 22.0, 23.7, 25.9, 29.5, 39.3, 41.2, 45.1, 58.8, 70.8, 73.2, 127.5, 127.6, 128.3, 138.4 ppm. HRMS (ES+): calcd. for $C_{16}H_{26}NO$ $[M + H]^+$ 248.2017; found 248.2023.

(2*S*,3*S*)-3-(Benzyloxymethyl)-2-[3-(*tert*-butyldimethylsilyloxy)-propyl]pyrrolidine (3k): Colourless oil (290 mg, 80%). $[\alpha]_D^{20}$ = +12.3 (*c* = 1, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.05 [s, 6 H, CH-(CH_3)$_2$], 0.91 [s, 9 H, C-$(CH_3)_3$], 1.36–1.71 [m, 5 H, SiOCH_2-(CH_2)$_2$, 4-H pyrrolidine], 1.91 (m, 1 H, 4-H pyrrolidine), 2.04 (br. s, 1 H, NH), 2.27 (m, 1 H, 3-H pyrrolidine), 2.78 (ddd, $^2J_{H,H}$ = 9.2, $^3J_{H,H}$ = 8.7, 7.3 Hz, 1 H, 5-H pyrrolidine), 2.92–3.06 (m, 2 H, 2-H, 5′-H pyrrolidine), 3.36 (d, $^2J_{H,H}$ = 9.0, $^3J_{H,H}$ = 6.7 Hz, 1 H, C$H_A$$H_B$OBn), 3.46 (dd, $^2J_{H,H}$ = 9.0, $^3J_{H,H}$ = 6.0 Hz, 1 H, $CH_A$$H_B$OBn), 3.56–3.64 (m, 2 H, CH_2OSi), 4.45 (s, 2 H, PhCH_2O), 7.25–7.30 (m, 5 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.4, 18.2, 25.9, 26.7, 29.4, 31.1, 41.0, 45.1, 61.1, 63.2, 70.7, 73.1, 127.4, 127.5, 128.2, 138.0 ppm. HRMS (ES+): calcd. for $C_{21}H_{38}NO_2Si$ $[M + H]^+$ 364.2672; found 364.2674.

(2*S*,3*S*)-[2-(3-Methylbutyl)pyrrolidin-3-yl]methanol Hydrochloride (3′i): Colourless oil (186 mg, 96%). $[\alpha]_D^{20}$ = +14.4 (*c* = 2, MeOH). ^1H NMR (250 MHz, CD_3OD): δ = 0.79 [d, $^3J_{H,H}$ = 5.6 Hz, 6 H, (CH_3)$_2$–CH], 1.49 (m, 3 H, CH_2-*i*Pr, 4-H pyrrolidine), 1.85–2.21 [m, 3 H, $(CH_3)_2$–CH, 3-H, 4-H pyrrolidine], 3.09 (m, 1 H, 5-H pyrrolidine), 3.21 (dt, $^2J_{H,H}$ = 11.0, $^3J_{H,H}$ = 8.6 Hz, 1 H, 5′-H pyrrolidine), 3.41 (m, 2 H, 2-H pyrrolidine, C$H_A$$H_B$OH), 3.51 (dd, $^2J_{H,H}$ = 10.8, $^3J_{H,H}$ = 4.3 Hz, 1 H, $CH_A$$H_B$OH) ppm. ^{13}C NMR (62.5 MHz, CD_3OD): δ = 22.4, 23.4, 26.6, 28.5, 37.2, 42.6, 44.9, 61.4, 61.7 ppm. HRMS (ES+): calcd. for $C_9H_{20}NO$ $[M – Cl]^+$ 158.1545; found 158.1542.

***tert*-Butyl (2*R*,3*S*)-3-(Hydroxymethyl)-2-hexylpyrrolidine-1-carboxylate (3l):** A mixture of **2l** (1.26 g, 3 mmol) and $Pd(OH)_2/C$ (20%, 300 mg) in MeOH (15 mL) under hydrogen was stirred overnight at room temp. The crude mixture was filtered through a pad of Celite and concentrated under reduced pressure. The residue was diluted in CH_2Cl_2 (20 mL) then Et_3N (0.46 mL) and Boc_2O (785 mg, 3.6 mmol) were added and the reaction mixture was stirred for 6 h at room temp. Then the solvent was removed under vacuum. The residue was diluted into THF (15 mL) and a solution of TBAF (1 M in THF, 9 mL) was added dropwise. After 2 h of stirring, the solvent was removed under vacuum and the residue was purified by flash chromatography on silica gel eluting with a mixture of PE/AcOEt (1:1) to give **3l** as a pale-yellow oil (996 mg, 83%). $[\alpha]_D^{20}$ = –3.6 (*c* = 1, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.82 (t, $^3J_{H,H}$ = 6.6 Hz, 3 H, CH_3), 1.22 [br. s, 9 H, $(CH_3)_3$-C], 1.37–1.44 [m, 10 H, $(CH_2)_5$], 1.58 (m, 1 H, 4-H pyrrolidine), 1.90 (m, 1 H, 4-H pyrrolidine), 2.32 (m, 1 H, 3-H pyrrolidine), 2.69 (br. s, 1 H, OH), 3.31 (br. d, $^3J_{H,H}$ = 8.0 Hz, 2 H, CH_2OH), 3.60 (m, 2 H, 5-H, 2-H pyrrolidine), 3.91 (m, 1 H, 5′-H pyrrolidine) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 14.0, 22.5, 25.5, 26.6, 28.4, 29.7, 29.9, 31.8, 44.5, 45.0, 57.9, 61.9, 79.1, 155.0 ppm. HRMS (ESI): calcd. for $C_{16}H_{31}NNaO_3$ $[M + Na]^+$ 308.2202; found 308.2216.

General Procedure for the Preparation of Boc-Protected Pyrrolidines 4 (Method E): $Pb(OAc)_4$ (2.18 g, 4.9 mmol) was added in one portion to a solution of homoallylic amine **1** (4.5 mmol) in a 1:1 mixture of CH_2Cl_2/MeOH (50 mL) at 0 °C. The resulting mixture was stirred at 0 °C for 30 min and then $NH_2OH·HCl$ (3.2 g, 45 mmol) was added and the stirring was continued for 30 min at 0 °C. The solvent was then removed under reduced pressure. The residue was taken up with CH_2Cl_2 (50 mL) and the solid was filtered off. Et_3N (1.25 mL) and Boc_2O (1.07 g, 4.9 mmol) were added to the filtrate and the resulting mixture was stirred at room temp. for 2 h. H_2O (20 mL) was added and the organic layer was washed with HCl (1 M, 10 mL) and Na_2CO_3 (10%, 10 mL), dried with $MgSO_4$, filtered and the solvent was removed under reduced pressure. The residue was purified on silica gel eluting with a mixture of PE/AcOEt to give compound **4**.

***tert*-Butyl (2*R*,3*R*)-[2-Phenyl-1-(3-pyridyl)but-3-enyl]carbamate (4b):** Obtained starting from a 20:1 mixture of diastereomers as a white solid (845 mg, 58%); m.p. 176 °C, *ee* = 90%. $[\alpha]_D^{20}$ = –48 (*c* = 1, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = 1.31 [s, 9 H, $(CH_3)_3$-C], 3.68 (m, 1 H, CH–CH=CH_2), 5.07 (m, 4 H, CHNHBoc, CH=CH_2), 5.90 (m, 1 H, CH=CH_2), 7.06–7.37 (m, 7 H, Ar-H), 8.35 (s, 1 H, 2-H pyridine), 8.47 (d, $^3J_{H,H}$ = 3.7 Hz, 1 H, 6-H pyridine) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 28.6, 55.9, 57.2, 80.3, 118.8, 123.3, 127.6, 128.7, 129.1, 135.2, 136.8, 139.7, 148.9, 149.3, 155.2 ppm (1 C is missing). HRMS (ES+): calcd. for $C_{20}H_{25}N_2O_2$ $[M + H]^+$ 325.1916; found 325.1919.

***tert*-Butyl (2*R*,3*R*)-[2-[(*tert*-Butyldimethylsilyloxy)methyl]-1-(2-furyl)but-3-enyl]carbamate (4c):** Colourless oil (1.14 g, 65%). $[\alpha]_D^{20}$ = +24 (*c* = 1, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = –0.01 (s, 3 H, CH_3Si–CH_3), 0.00 (s, 3 H, CH_3Si–CH_3), 0.88 [s, 9 H, $(CH_3)_3$CSi], 1.9 [s, 9 H, $(CH_3)_3$C-O], 2.63 (m, 1 H, CH–CH=CH_2), 3.56 (d, $^3J_{H,H}$ = 3.8 Hz, 2 H, CH_2OSi), 4.94 (dd, $^3J_{H,H}$ = 7.7, 5.2 Hz, 1 H, CH-NHBoc), 5.11–5.21 (m, 2 H, CH=CH_2), 5.78 (m, 1 H, CH=CH_2), 5.88 (m, 1 H, NH), 6.14 (s, 1 H, furyl-H), 6.27 (s, 1 H, furyl-H), 7.29 (s, 1 H, furyl-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.8, –5.7, 18.0, 25.8, 28.3, 48.1, 51.1, 63.8, 79.0, 106.5, 110.0, 117.7, 135.8, 141.4, 154.3, 155.3 ppm. HRMS (ES+): calcd. for $C_{20}H_{35}NNaO_4Si$ $[M + Na]^+$ 404.2233; found 404.2243.

***tert*-Butyl (2*R*,3*R*)-[2-[(*tert*-Butyldimethylsilyloxy)methyl]-1-phenylbut-3-enyl]carbamate (4d):** Obtained starting from a 9.2:1 mixture of diastereoisomers as a colourless oil (1.28 g, 73%). *ee* = 80%. $[\alpha]_D^{20}$ = +0.4 (*c* = 1, CH_2Cl_2). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.00 [s, 6 H, $(CH_3)_2$Si], 0.91 [s, 9 H, $(CH_3)_3$CSi], 1.49 [s, 9 H, $(CH_3)_3$C-O], 2.41 (m, 1 H, CH–CH=CH_2), 3.49 (m, 2 H, CH_2OSi),

4.87 (m, 1 H, C*H*NHBoc), 5.13 (d, $^3J_{H,H}$ = 10.0 Hz, 1 H, CH=CH_AH$_B$), 5.16 (d, $^3J_{H,H}$ = 17.5 Hz, 1 H, CH=CH$_A$*H*$_B$), 5.84 (m, 1 H, C*H*=CH$_2$), 6.35 (br. d, $^3J_{H,H}$ = 6.0 Hz, 1 H, NH), 7.20–7.28 (m, 5 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.7, 18.0, 25.8, 27.4, 28.4, 49.6, 57.2, 63.3, 117.2, 126.5, 126.8, 128.1, 136.7, 141.6, 155.4 ppm. HRMS (ESI): calcd. for $C_{22}H_{38}NO_3Si$ [M + H]$^+$ 392.2621; found 392.2612.

***tert*-Butyl [(2*R*,3*R*,*E*)-2-(Benzyloxymethyl)-1-styrylbut-3-enyl]-carbamate (4e):** White solid (1.27 g, 72%); m.p. 76 °C. $[\alpha]_D^{20}$ = +35.3 (*c* = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.39 [s, 9 H, $(CH_3)_3$C-O], 2.55 (m, 1 H, C*H*–CH=CH$_2$), 3.46 (m, 2 H, C*H*$_2$OBn), 4.37 (d, $^2J_{H,H}$ = 12.0 Hz, 1 H, OC*H*$_A$H$_B$Ph), 4.39 (d, $^2J_{H,H}$ = 12.0 Hz, 1 H, OC*H*$_A$H$_B$Ph), 4.45 (br. s, 1 H, NH), 5.12 (d, $^3J_{H,H}$ = 10.2 Hz, 1 H, CH=CH_AH$_B$), 5.14 (d, $^3J_{H,H}$ = 17.8 Hz, 1 H, CH=CH$_A$*H*$_B$), 5.24 (br. d, $^3J_{H,H}$ = 8.0 Hz, 1 H, NHC*H*), 5.70 (dt, *J* = 17.8, 10.2 Hz, 1 H, C*H*=CH$_2$), 5.99 (dd, $^3J_{H,H}$ = 15.9, 6.3 Hz, 1 H, Ph–CH=C*H*), 6.44 (d, $^3J_{H,H}$ = 15.9 Hz, 1 H, Ph–CH=CH), 7.14–7.24 (m, 10 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 27.6, 28.2, 53.4, 70.5, 73.0, 78.9, 118.3, 126.2, 127.2, 127.4, 127.7, 127.9, 128.15, 128.25, 130.8, 135.4, 136.6, 137.8, 155.0 ppm. HRMS (ESI): calcd. for $C_{25}H_{31}NO_3Na$ [M + Na]$^+$ 416.2202; found 416.2205.

***tert*-Butyl [(2*R*,3*R*,*E*)-2-[(*tert*-Butyldimethylsilyloxy)methyl]-1-styrylbut-3-enyl]carbamate (4f):** Colourless oil (1.22 g, 72%). $[\alpha]_D^{20}$ = +38.2 (*c* = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.06 [s, 6 H, $(CH_3)_2$Si], 0.93 [s, 9 H, $(CH_3)_3$CSi], 1.45 [s, 9 H, $(CH_3)_3$C-O], 2.45 (m, 1 H, C*H*–CH=CH$_2$), 3.67 (m, 1 H, C*H*$_A$H$_B$OSi), 3.80 (m, 1 H, C*H*$_A$H$_B$OSi), 4.53 (m, 1 H, C*H*NHBoc), 5.22 (d, $^3J_{H,H}$ = 18.5 Hz, 1 H, CH=CH_AH$_B$), 5.24 (d, $^3J_{H,H}$ = 9.0 Hz, 1 H, CH=CH$_A$*H*$_B$), 5.60 (br. d, *J* = 6.8 Hz, 1 H, NH), 5.83 (m, 1 H, C*H*=CH$_2$), 6.14 (dd, $^3J_{H,H}$ = 15.8, 6.0 Hz, 1 H, PhCH=C*H*), 6.55 (d, $^3J_{H,H}$ = 15.8 Hz, 1 H, PhC*H*=CH), 7.18–7.38 (m, 5 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.7, –5.6, 18.1, 25.8, 28.4, 49.3, 54.1, 63.8, 78.9, 117.9, 126.4, 127.3, 128.4, 128.6, 130.6, 136.1, 137.0, 155.3 ppm. HRMS (ESI): [M + Na]$^+$ calcd. for $C_{24}H_{39}NO_3SiNa$ 400.2597; found 400.2592.

General Procedure for the Preparation of Boc-Protected Pyrrolidines 5 (Method F): $Cp_2Zr(H)Cl$ (772 mg, 3 mmol) was added in one portion to a solution of **4** (1 mmol) in CH_2Cl_2 (3 mL) under argon and the resulting mixture was stirred until complete dissolution. Then I_2 (254 mg, 1 mmol) was added and the reaction mixture was stirred for 2 h. CH_2Cl_2 (10 mL) was added and the organic phase was washed with HCl (1 M, 2 × 3 mL) and Na_2CO_3 (10%, 2 × 3 mL), dried with $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude material was dissolved in THF (10 mL) and NaHMDS (1 M in THF, 1.5 mL) was added dropwise at 0 °C. The resulting mixture was stirred for 2 h at room temp. Then Et_2O (10 mL) and H_2O (10 mL) were added. The aqueous layer was extracted with Et_2O (2 × 5 mL). The combined organic layers were washed with HCl (1 M, 5 mL) and Na_2CO_3 (10%, 5 mL), dried with $MgSO_4$, filtered and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with a mixture of PE/AcOEt to give compound **5**.

***tert*-Butyl (2*R*,3*R*)-3-Phenyl-2-(3-pyridyl)pyrrolidine-1-carboxylate (5b):** Yellow oil (1.55 mg, 48%). *ee* = 90%. $[\alpha]_D^{20}$ = –168 (*c* = 0.35, CH_2Cl_2). 1.6:1 mixture of rotamers. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.20 [s, 5.54 H, $(CH_3)_3$C-O, major], 1.48 [s, 3.46 H, $(CH_3)_3$C-O minor], 2.10–2.19 (m, 1 H, 4-H pyrrolidine), 2.27–2.46 (m, 1 H, 4′-H pyrrolidine), 3.59–4.02 (m, 3 H, 5-H, 3-H pyrrolidine), 5.01 (d, *J* = 7.8 Hz, 0.62 H, 2-H pyrrolidine major), 5.08 (d, *J* = 7.8 Hz, 0.38 H, 2-H pyrrolidine minor), 6.80 (m, 2 H, pyridine-H), 6.95–7.11 (m, 5 H, Ar-H), 7.98 (s, 0.62 H, 2-H pyridine minor), 8.08 (s, 0.38 H, 2-H pyridine minor), 8.32 (m, 1 H, 6-H pyridine) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 26.3 (major), 26.9 (minor), 28.1 (major), 28.4 (minor), 45.9 (major), 46.4 (minor), 49.0 (minor), 49.7 (major), 63.0 (minor), 63.3 (major), 79.7 (major), 79.9 (minor), 122.4 (minor + major), 127.1 (minor + major), 128.1 (minor + major), 128.3 (minor + major, 2 C), 134.1 (major), 134.8 (minor), 136.0 (minor), 136.9 (major), 147.9 (major + minor), 148.3 (major + minor), 154.0 (major), 154.2 (minor) ppm. HRMS (ESI): calcd. for $C_{20}H_{25}N_2O_2$ [M + H]$^+$ 325.1916; found 325.1911.

***tert*-Butyl (2*R*,3*R*)-3-[(*tert*-Butyldimethylsilyloxy)methyl]-2-(2-furyl)pyrrolidine-1-carboxylate (5c):** Yellow oil (198 mg, 52%). $[\alpha]_D^{20}$ = –6.7 (*c* = 1, CH_2Cl_2). 1.8:1 mixture of rotamers. ^{1}H NMR (250 MHz, $CDCl_3$): δ = –0.01 [s, 2.1 H, $(CH_3)_2$Si minor], 0.00 [s, 3.9 H, $(CH_3)_2$Si minor], 0.90 [s, 9 H, $(CH_3)_3$CSi], 1.34 [s, 5.85 H, $(CH_3)_3$CO, major], 1.48 [s, 3.15 H, $(CH_3)_3$CO minor], 1.86–2.09 (m, 2 H, 4-H pyrrolidine), 2.62 (m, 1 H, 3-H pyrrolidine), 3.03–3.49 (m, 3 H, 5-H pyrrolidine, CH_2OSi), 3.63–3.80 (m, 1 H, 5′-H pyrrolidine), 4.91 (d, $^3J_{H,H}$ = 7.5 Hz, 0.65 H, 2-H pyrrolidine major), 4.91 (d, $^3J_{H,H}$ = 7.3 Hz, 0.35 H, 2-H pyrrolidine major), 6.11 (s, 0.65 H, furyl-H major), 6.21 (m, 0.35 H, furyl-H major), 6.33 (m, 1 H, furyl-H), 7.34 (m, 1 H, 5-H furyl major) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.7 (major), –5.6 (minor), 25.8, 26.0 (major), 26.9 (minor), 28.2 (major), 28.4 (minor), 45.2 (major), 45.8 (minor), 45.9 (minor), 46.6 (major), 55.9 (minor), 56.4 (major), 62.7, 79.2, 106.9, 107.4, 109.8 (major), 110.0 (minor), 141.0 (major), 141.2 (minor), 154.0 (major), 154.2 (minor) ppm. HRMS (ESI): calcd. for $C_{20}H_{35}NO_4SiNa$ [M + Na]$^+$ 404.2233; found 404.2239.

***tert*-Butyl (2*R*,3*R*)-3-[(*tert*-Butyldimethylsilyloxy)methyl]-2-phenylpyrrolidine-1-carboxylate (5d):** Pale-yellow oil (266 mg, 68%). *ee* = 80%. $[\alpha]_D^{20}$ = –19.8 (*c* = 1, CH_2Cl_2). 2:1 mixture of rotamers. ^{1}H NMR (250 MHz, $CDCl_3$): δ = –0.08 [s, 6 H, $(CH_3)_2$Si], 0.86 [s, 9 H, $(CH_3)_3$CSi], 1.15 [s, 6 H, $(CH_3)_3$C-O, major], 1.43 [s, 3 H, $(CH_3)_3$C-O, minor], 1.70 (m, 1 H, 4-H pyrrolidine), 1.93 (m, 1 H, 4-H pyrrolidine), 2.63 (m, 1 H, 3-H pyrrolidine), 2.98–3.15 (m, 2 H, CH_2OSi), 3.43–3.85 (m, 2 H, 5-H pyrrolidine), 4.88 (d, $^3J_{H,H}$ = 8.0 Hz, 0.67 H, 2-H pyrrolidine major), 5.05 (d, $^3J_{H,H}$ = 7.5 Hz, 0.33 H, 2-H pyrrolidine minor), 7.10–7.28 (m, 5 H, Ph-H) ppm. Major rotamer: ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.2, –5.0, 18.6, 25.7, 28.5, 46.2, 47.1, 63.2, 63.3, 79.4, 127.1, 127.5, 128.1, 141.4, 154.8 ppm. HRMS (ESI): calcd. for $C_{22}H_{38}NO_3Si$ [M + H]$^+$ 392.2621; found 392.2619.

***tert*-Butyl (2*R*,3*R*)-3-(Benzyloxymethyl)-2-styrylpyrrolidine-1-carboxylate (5e):** Yellow oil (303 mg, 77%). $[\alpha]_D^{20}$ = +0.7 (*c* = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.39 [s, 9 H, $(CH_3)_3$CO], 1.64 (m, 1 H, 4-H pyrrolidine), 1.93 (m, 1 H 4′-H pyrrolidine), 2.62 (m, 1 H, 3-H pyrrolidine), 3.33–3.45 (m, 3 H, CH_2OBn, 5-H pyrrolidine), 3.59 (app. t, $J_{H,H}$ = 9.7 Hz, 1 H, 5′-H pyrrolidine), 4.42 (d, $^2J_{H,H}$ = 12.0 Hz, 1 H, PhC*H*$_A$H$_B$O), 4.51 (d, $^2J_{H,H}$ = 12.0 Hz, 1 H, PhCH$_A$*H*$_B$O), 4.61 (m, 1 H, 2-H pyrrolidine), 6.01 (dd, $^3J_{H,H}$ = 15.5, 6.7 Hz, 1 H, PhCH=C*H*), 6.40 (d, $^3J_{H,H}$ = 15.5 Hz, 1 H, PhC*H*=CH), 7.27–7.29 (m, 10 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 25.2, 28.3, 43.5, 45.0, 60.5, 69.7, 73.2, 79.0, 126.2 (2 C), 127.2, 127.5, 127.6, 128.2, 128.4, 131.1, 136.8, 137.9, 154.4 ppm. HRMS (ESI): calcd. for $C_{25}H_{31}NO_3Na$ [M + Na]$^+$ 416.2202; found 416.2204.

***tert*-Butyl (2*R*,3*R*)-3-[(*tert*-Butyldimethylsilyloxy)methyl]-2-styrylpyrrolidine-1-carboxylate (5f):** Yellow oil (339 mg, 90%). $[\alpha]_D^{20}$ = –1.2 (*c* = 1, CH_2Cl_2). 1.8:1 mixture of rotamers. Major rotamer: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.03 [s, 6 H, $(CH_3)_2$Si], 0.90 [s, 9 H, $(CH_3)_3$CSi], 1.40 [s, 9 H, $(CH_3)_3$C-O], 1.64 (app. quint, $J_{H,H}$

= 10.2 Hz, 1 H, 4-H pyrrolidine), 1.91 (m, 1 H, 4′-H pyrrolidine), 2.51 (m, 1 H, 3-H pyrrolidine), 3.40 (m, 1 H, 5-H pyrrolidine), 3.58 (m, 3 H, 5′-H pyrrolidine CH_2OSi), 4.48 (t, $^3J_{H,H}$ = 6.8 Hz, 1 H, 2-H pyrrolidine), 6.06 (dd, $^3J_{H,H}$ = 15.5, 6.9 Hz, 1 H, Ph–CH=C*H*), 6.39 (d, $^3J_{H,H}$ = 15.5 Hz, 1 H, Ph–CH=CH), 7.20–7.38 (m, 5 H, Ph-H) ppm. Major rotamer: ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.5, 18.1, 25.4, 25.8, 28.4, 45.2, 46.1, 60.6, 62.6, 79.1, 126.2, 128.4, 131.1, 137.0, 154.5 ppm (2 C are missing). HRMS (ESI): calcd. for $C_{24}H_{39}NNaO_3Si$ $[M + Na]^+$ 400.2597; found 400.2590.

General Procedure for the Preparation of β-Proline Analogues 6d and 6l (Method G): A solution of TBAF (1 M in THF, 1.5 mL) was added to a solution of **5d** (391 mg, 1 mmol) in THF (5 mL) at room temp. The resulting mixture was stirred for 2 h and then the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (20 mL), washed with water (3 × 10 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure to give quantitatively **5′d**.

$RuCl_3{\cdot}H_2O$ (6.2 mg, 0.1 mmol) was added to a solution of **5′d** or **3l** (1 mmol) in a 2:2:3 mixture of $CCl_4/CH_3CN/H_2O$ (14 mL) and the resulting black mixture was stirred for 10 min. Then $NaIO_4$ (1.28 g, 6 mmol) was added in one portion and the stirring was continued for 2 h. Water (5 mL) and CH_2Cl_2 (5 mL) were added. The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL), the organic phases were combined, dried with $NaSO_4$, filtered and concentrated under reduced pressure. The residue was filtered through a pad of silica eluting with AcOEt to give the corresponding acid.

(2*R*,3*S*)-1-(*tert*-Butoxycarbonyl)-2-phenylpyrrolidine-3-carboxylic Acid (6d): Yellow oil (250 mg, 86%). $[\alpha]_D^{20}$ = –3.7 (*c* = 1, CH_2Cl_2). 2.75:1 mixture of rotamers/ ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.12 [s, 6.6 H, $(CH_3)_3$C-O, major], 1.40 [s, 2.4 H, $(CH_3)_3$C-O, minor], 1.99 (m, 1 H, 4-H pyrrolidine), 2.31 (app. quint, *J* = 10.9 Hz, 1 H, 4′-H pyrrolidine), 3.29–3.48 (m, 2 H, 5-H pyrrolidine), 3.77 (t, $^3J_{H,H}$ = 9.4 Hz, 1 H, 3-H pyrrolidine), 5.04 (d, $^3J_{H,H}$ = 8.4 Hz, 0.63 H, 2-H pyrrolidine minor), 5.19 (d, $^3J_{H,H}$ = 7.5 Hz, 0.37 H, 2-H pyrrolidine minor), 7.06–7.24 (m, 5 H, Ph-H), 9.03 (br. s, 1 H, CO_2H) ppm. Major rotamer: ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 24.0, 28.0, 45.5, 49.4, 62.2, 79.9, 126.7, 127.3, 127.8, 139.8, 154.2, 174.6 ppm. HRMS (ESI): calcd. for $C_{16}H_{20}NO_4$ $[M - H]^+$ 290.1392; found 290.1398.

(2*R*,3*S*)-1-(*tert*-Butoxycarbonyl)-2-hexylpyrrolidine-3-carboxylic Acid (6l): Yellow oil (67%). $[\alpha]_D^{20}$ = +3.7 (*c* = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.85 (m, 3 H, CH_3), 1.23 [m, 10 H, $(CH_2)_5$], 1.44 [s, 9 H, $(CH_3)_3$C-O], 2.05 (m, 1 H, 4-H pyrrolidine), 2.35 (m, 1 H, 4′-H pyrrolidine), 3.09 (dt, $^3J_{H,H}$ = 11.8, 7.1 Hz, 1 H, 3-H pyrrolidine), 3.40 (br. m, 2 H, 5-H pyrrolidine), 4.18 (br. m, 1 H, 2-H pyrrolidine), 9.27 (br. s, 1 H, CO_2H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 14.0, 22.4, 24.4, 26.4, 28.4, 29.4, 31.2, 21.7, 44.2, 47.2, 58.0, 79.9, 154.6, 176.5 ppm. HRMS (ESI): calcd. for $C_{16}H_{28}NNaO_4$ $[M - H]^+$ 298.2018; found 298.2005.

Methyl (2*R*,3*S*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butyldimethylsilyloxy)methyl]pyrrolidine-2-carboxylate (6f): $RuCl_3{\cdot}H_2O$ (22 mg, 0.1 mmol) was added to a solution of **5f** (417 mg, 1 mmol) in a 2:2:3 mixture of $CCl_4/CH_3CN/H_2O$ (14 mL) and the resulting black mixture was stirred for 10 min. Then $NaIO_4$ (1.28 g, 6 mmol) was added in one portion and the stirring was continued for 2 h. Water (5 mL) and CH_2Cl_2 (5 mL) were added. The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL) and the organic phases were combined, dried with $NaSO_4$, filtered and concentrated under reduced pressure. The residue was diluted in a 5:1 mixture of Et_2O/MeOH (18 mL) and a solution of $TMSCHN_2$ (2 M in Et_2O, 0.6 mL) was added dropwise. The stirring was continued for 30 min and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with a mixture of PE/AcOEt to give **6f** as a yellow oil (239 mg, 64%). $[\alpha]_D^{20}$ = –4.2 (*c* = 1, CH_2Cl_2). 1.4:1 mixture of rotamers. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.00 [s, 6 H, $(CH_3)_2$Si], 0.86 [s, 9 H, $(CH_3)_3$CSi], 1.38 [s, 5.3 H, $(CH_3)_3$C-O, major], 1.43 [s, 3.7 H, $(CH_3)_3$C-O, minor], 1.80–1.98 (m, 2 H, 4-H pyrrolidine), 2.55 (m, 1 H, 3-H pyrrolidine), 3.33 (m, 1 H, 5-H pyrrolidine), 3.47 (dd, $^2J_{H,H}$ = 10.1, $^3J_{H,H}$ = 6.8 Hz, 1 H, C*H*$_A$H$_B$OSi), 3.62 (m, 2 H, 5′-H pyrrolidine, CH$_A$*H*$_B$OSi), 3.66 (s, 3 H, OCH_3), 4.23 (d, $^3J_{H,H}$ = 8.5 Hz, 0.6 H, 2-H pyrrolidine major), 4.32 (d, $^3J_{H,H}$ = 8.4 Hz, 0.4 H, 2-H pyrrolidine minor) ppm. Major rotamer: ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.5, 18.2, 25.8, 26.4, 28.2, 45.2, 45.5, 51.5, 60.7, 61.9, 62.0, 79.8, 153.7, 172.0 ppm. HRMS (ESI): calcd. for $C_{18}H_{35}NO_5SiNa$ $[M + Na]^+$ 396.2182; found 396.2172.

(1*S*,7a*S*)-1-(Benzyloxymethyl)hexahydro-1*H*-pyrrolizine (3′k): TBAF (1 M in THF, 1.8 mL) was added dropwise to a solution of **3k** (440 mg, 1.2 mmol) in THF (12 mL) at 0 °C under argon. The reaction mixture was stirred for 6 h at room temp. and the solvent was removed under reduced pressure. The residue (240 mg) was diluted in CH_2Cl_2 (6 mL) and then Et_3N (3 mL), PPh_3 (300 mg, 1.5 mmol) and CBr_4 (280 mg, 1.5 mmol) were successively added at 0 °C. The reaction mixture was stirred at 0 °C for 2 h. CH_2Cl_2 (10 mL) was added and the reaction mixture was washed with an aqueous solution of NaOH (2 M, 5 mL). The organic layer was dried with $MgSO_4$, filtered and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using Et_2O/Et_2NH gradient elution (100:0→80:20) to give the corresponding amine (139 mg, 50%). $[\alpha]_D^{20}$ = –54.8 (*c* = 1, MeOH). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.33 (m, 1 H), 1.52 (m, 1 H), 1.60–1.87 (m, 4 H), 2.45 (dt, $^2J_{H,H}$ = 9.5, $^3J_{H,H}$ = 6.5 Hz, 1 H), 2.51–2.62 (m, 2 H), 2.99 (ddd, $^2J_{H,H}$ = 10.9, $^3J_{H,H}$ = 9.1, 6.3 Hz, 1 H), 3.13 (ddd, $^2J_{H,H}$ = 10.2, $^3J_{H,H}$ = 7.1, 3.3 Hz, 1 H), 3.44–3.57 (m, 3 H, C*H*$_2$OBn, 2-H pyrrolidine), 4.51 (s, 2 H, PhC*H*$_2$O), 7.29–7.35 (m, 5 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 26.1, 26.5, 27.5, 41.4, 54.0, 55.7, 66.2, 71.2, 73.1, 127.4, 127.5, 128.2, 138.3 ppm. HRMS (ESI): calcd. for $C_{15}H_{22}NO$ $[M + Na]^+$ 232.1696; found 232.1701.

[(1*S*,7a*S*)-Hexahydro-1*H*-pyrrolizin-1-yl]methanol Hydrochloride [(–)-Isoretronecanol]: A mixture of **3′k** (82 mg, 0.29 mmol) and $Pd(OH)_2$/C (20%, 35 mg) in a mixture of MeOH (5 mL) and HCl (6 N, 50 μL) under hydrogen was stirred overnight at room temp. The crude mixture was filtered through a pad of Celite and concentrated under reduced pressure to give the title compound (45 mg, 87%). $[\alpha]_D^{20}$ = –38.5 (*c* = 1, MeOH). ^{1}H NMR (250 MHz, CD_3OD): δ = 1.75–1.89 (m, 3 H), 1.94–2.14 (m, 3 H), 2.52 (m, 1 H), 2.92 (app. td, $J_{H,H}$ = 10.9, 5.9 Hz, 1 H), 3.21 (m, 2 H), 3.36 (app. td, $J_{H,H}$ = 11.7, 5.3 Hz, 1 H, C*H*$_A$H$_B$N), 3.52–3.71 (m, 3 H, C*H*$_2$OH, CH$_A$*H*$_B$N), 4.11 (dt, $^3J_{H,H}$ = 9.1, 8.0 Hz, 1 H, CHN) ppm. ^{13}C NMR (62.5 MHz, CD_3OD): δ = 26.4, 27.0, 27.1, 44.2, 55.1, 57.0, 61.5, 71.1 ppm. HRMS (ESI): calcd. for $C_8H_{16}NO$ $[M + H]^+$ 142.1232; found 142.1228.

***tert*-Butyl (2*R*,3*S*)-3-(Benzyloxymethyl)-2-[(*R*)-1-hydroxybut-3-enyl]-1-pyrrolidine-1-carboxylate (7):** A solution of OsO_4 (4% in water, 1.6 mL) was added to a solution of **5e** (1.16 g, 2.95 mmol) in a 2:1 mixture of THF/H_2O (90 mL) and the resulting mixture was stirred for 15 min. $NaIO_4$ (3.15 g, 14.6 mmol) was then added in one portion and the stirring was continued for 3 h. Water (50 mL) and CH_2Cl_2 (50 mL) were added. The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL) and then the combined organic phases were washed with brine (100 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude material was diluted in a 1:1 mixture of THF/MeOH (15 mL) cooled to 0 °C

and then allyl bromide (1.5 mL, 18 mmol) and In (690 mg, 6 mmol) were added. The resulting mixture was stirred for 6 h at room temp. and then a saturated aqueous solution of $NaHCO_3$ (15 mL) was added. The solid was filtered off, the aqueous layer was extracted with AcOEt (3 × 20 mL) and the combined organics phases were dried with $MgSO_4$, filtered and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using PE/AcOEt gradient elution (95:5→80:20) to give the corresponding alcohol (680 mg, 64%) as an 8:1 mixture of diastereomers.

The major diastereoisomer was isolated in pure form as a yellow oil (415 mg, 39%). $[\alpha]_D^{20}$ = +26.5 (*c* = 2, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.46 [s, 9 H, $(CH_3)_3C$], 1.81–2.25 (m, 4 H, 3-H, 4-H pyrrolidine, C*H*$_A$H$_B$–CH=CH$_2$), 2.37–2.58 (m, 2 H, CH$_A$*H*$_B$–CH=CH$_2$, OH), 3.62–3.74 (m, 4 H, C*H*$_2$OBn, 5-H pyrrolidine), 3.63 (br. s, 1 H, C*H*NBoc), 3.95 (br. d, $^3J_{H,H}$ = 6.1 Hz, 1 H, C*H*OH), 4.53 (s, 2 H, PhC*H*$_2$O), 5.07–5.13 (m, 2 H, CH=C*H*$_2$), 5.88 (m, 1 H, C*H*=CH$_2$), 7.28–7.38 (m, 5 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 26.5 (br.), 28.4, 40.1, 41.8 (br.), 46.3, 61.4, 69.1, 71.3 (br.), 73.2, 79.4 (br.), 117.2, 127.7, 128.3 (2 C), 135.7, 137.7 ppm (1 C is missing). HRMS (ESI): calcd. for $C_{21}H_{31}NO_4Na$ [M + Na]$^+$ 384.2151; found 384.2155.

(1*R*,7*S*,7a*R*)-1-Allyl-7-(benzyloxymethyl)-5,6,7,7a-tetrahydropyrrolo[1,2-*c*]oxazol-3(1*H*)-one (7′): A solution of NaHMDS (1 M in THF, 0.25 mL) was added to a solution of **7** (82 mg, 0.23 mmol) in THF (5 mL) at 0 °C and the resulting mixture was stirred for 2 h at room temp. Water (5 mL) was added and the organic layer was washed with HCl (1 M, 5 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure to give **7′** (52 mg, 78%) after purification by flash chromatography on silica gel eluting with a 1:1 mixture of PE/AcOEt. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.79 (m, 1 H, 4-H pyrrolidine), 2.08 (m, 1 H, 4′-H pyrrolidine), 2.37–2.60 (m, 3 H, C*H*$_2$–CH=CH$_2$, 3-H pyrrolidine), 3.10 (ddd, $^2J_{H,H}$ = 11.2, $^3J_{H,H}$ = 8.8, 5.2 Hz, 1 H, 5-H pyrrolidine), 3.34–3.43 (m, 2 H, C*H*$_2$OBn), 3.62 (dt, $^2J_{H,H}$ = 11.1, $^3J_{H,H}$ = 8.0 Hz, 1 H, 5′-H pyrrolidine), 3.72 (dd, $^3J_{H,H}$ = 6.5, 4.1 Hz, 1 H, 2-H pyrrolidine), 4.44 (d, $^2J_{H,H}$ = 12.2 Hz, 1 H, PhC*H*$_A$H$_B$O), 4.50 (d, $^2J_{H,H}$ = 12.2 Hz, 1 H, PhCH$_A$*H*$_B$O), 4.71 (dt, $^3J_{H,H}$ = 6.2, 4.1 Hz, 1 H, C*H*OH), 5.16 (d, $^3J_{H,H}$ = 11.7 Hz, 1 H, CH=C*H*$_A$H$_B$), 5.17 (d, *J* = 15.7 Hz, 1 H, CH=C*H*$_A$H$_B$), 5.79 (ddt, *J* = 15.7, 11.7, 7.0 Hz, 1 H, C*H*=CH$_2$), 7.29–7.38 (m, 5 H, *H* Ph) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 26.7, 30.0, 39.6, 39.7, 44.5, 65.3, 69.5, 73.4, 75.0, 119.0, 127.8, 128.40, 128.45, 129.5, 131.7 ppm (1 C is missing). HRMS (ESI): calcd. for $C_{17}H_{21}NO_3Na$ [M + Na]$^+$ 310.1419; found 310.1409.

***tert*-Butyl (2*R*,3*S*)-2-[(*R*)-1-Benzyloxybut-3-enyl]-3-(benzyloxymethyl)pyrrolidine-1-carboxylate (8):** NaH (30 mg, 1.23 mmol), BnBr (0.1 mL, 0.82 mmol) and Bu_4NI (10 mg, 0.04 mol) were added in one portion to a solution of **7** (150 mg, 0.41 mmol) in THF (0.4 mL) at room temp. The solution was stirred for 10 h at room temp. and then water (1 mL) was added. The aqueous layer was extracted with Et_2O (3 × 2 mL) and the organic phases were combined, dried with Na_2SO_4, filtered and concentrated under reduced pressure to give **8** (96 mg, 52%) as a pale-yellow oil after purification by flash chromatography on silica gel using a 5:1 mixture of PE/AcOEt as eluent. $[\alpha]_D^{20}$ = +28 (*c* = 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.46 (s, 9 H), 1.67–1.94 (m, 2 H), 2.38–2.57 (m, 3 H), 3.04–3.60 (m, 5 H), 4.08–4.60 (m, 5 H), 5.04–5.16 (m, 2 H), 5.94 (m, 1 H), 7.14–7.32 (m, 10 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 26.7, 28.5, 35.7, 42.5, 45.9, 59.4, 70.9, 72.9, 73.3, 79.4, 79.7, 116.4, 127.2, 127.5, 127.6, 127.8, 128.2, 128.3, 135.9, 137.9, 138.6, 155.0 ppm. HRMS (ESI): calcd. for $C_{28}H_{37}NO_4Na$ [M + Na]$^+$ 474.2620; found 474.2628.

(1*S*,8*R*,8a*R*)-8-Benzyloxy-1-(benzyloxymethyl)octahydroindolizine (9): $Cp_2Zr(H)Cl$ (65 mg, 0.25 mmol) was added in one portion to a solution of **8** (95 mg, 0.21 mmol) in CH_2Cl_2 (1 mL) and the reaction mixture was stirred at room temp. until complete dissolution (ca. 2 h) and then I_2 (56 mg, 0.21 mmol) was added. The stirring was continued for 1 h and then CH_2Cl_2 (4 mL) and HCl (1 M, 1 mL) were added. The organic layer was washed with HCl (1 M, 2 × 1 mL), dried with $MgSO_4$ and filtered through a pad of silica gel. The filtrate was concentrated under reduced pressure. The residue (85 mg) was diluted in CH_2Cl_2 (15 mL) and then TFA (1.5 mL) was added at 0 °C and the resulting mixture was stirred for 2 h at room temp. The solvent and the excess TFA were removed under reduced pressure. The residue was diluted in CH_2Cl_2 (20 mL), solid $NaHCO_3$ (200 mg) was added and the mixture was stirred for 2 h at room temp. The solid was filtered off, the filtrate was washed with NaOH (2 M, 5 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure to give **9** as a yellow oil (45 mg, 61%), which was used in the next step without purification. $[\alpha]_D^{20}$ = –26.5 (*c* = 1, CH_2Cl_2). ^{1}H NMR: δ = 1.24 (m, 1 H, CH$_2$–CH$_A$H$_B$–CH$_2$), 1.42 (m, 1 H, CH$_2$–CH$_A$*H*$_B$–CH$_2$), 1.58 (m, 1 H), 1.91–2.23 (m, 6 H), 2.31 (d, $^3J_{H,H}$ = 8.5 Hz, 1 H), 2.54 (m, 1 H, C*H*$_A$H$_B$N), 3.14 (m, 2 H, CHN, CH$_A$*H*$_B$N), 3.51 (t, $^2J_{H,H}$ = $^3J_{H,H}$ = 8.9 Hz, 1 H, PhCH$_A$*H*$_B$O, 3.66 (dd, $^2J_{H,H}$ = 8.9, $^3J_{H,H}$ = 6.6 Hz, 1 H, CH$_A$*H*$_B$OBn), 3.78 (br. s, 1 H, CHO), 4.25 (d, $^2J_{H,H}$ = 11.4 Hz, 1 H, PhC*H*$_A$H$_B$O), 4.26 (s, 2 H, PhC*H*$_2$O), 4.51 (d, $^2J_{H,H}$ = 11.4 Hz, 1 H, PhCH$_A$*H*$_B$O), 7.24–7.35 (m, 10 H, Ph-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 18.6, 26.7, 27.6, 40.2, 52.4, 53.7, 70.7, 72.75, 72.80, 72.9, 127.3, 127.4, 127.6, 128.1, 128.2, 138.1, 138.6 ppm. HRMS (ESI): calcd. for $C_{23}H_{30}NO_2$ [M + H]$^+$ 352.2277; found 352.2280.

(1*S*,8*R*,8a*R*)-Octahydro-1-(hydroxymethyl)indolizin-8-ol (10): A solution of **9** (60 mg, 0.17 mmol) in MeOH (3 mL) and HCl (6 N, 0.05 mL) in the presence of Pd/C (10%, 30 mg) was stirred for 10 h under H_2. The crude mixture was filtered through a pad of Celite and concentrated under reduced pressure to give **10** (33 mg, 93%). $[\alpha]_D^{20}$ = –3.9 (*c* = 1, MeOH). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.34–1.52 (m, 3 H), 1.76–2.09 (m, 6 H), 2.34 (m, 1 H), 3.03–3.14 (m, 2 H), 3.55 (dd, $^2J_{H,H}$ = 11.8, $^3J_{H,H}$ = 4.2 Hz, 1 H, C*H*$_A$H$_B$OH), 3.67 (d, = 11.8, $^3J_{H,H}$ = 8.2 Hz, 1 H, CH$_A$*H*$_B$OH), 3.50–3.80 (br. s, 2 H, 2 OH), 4.22 (br. s, 1 H, C*H*OH) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 19.5, 24.8, 31.9, 42.1, 54.05, 54.15, 63.4, 65.8, 69.1 ppm. HRMS (ESI): calcd. for $C_9H_{18}NO_2$ [M + H]$^+$ 172.1338; found 172.1335.

Supporting Information (see also the footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of new compounds.

Acknowledgments

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[1] a) J. W. Daly, T. F. Spende, in: *Alkaloids: Chemical and Biological Perspectives* (Ed.: S. W. Pelletier), Wiley, New York, **1986**, vol. 4, chapter 1; b) J. C. Braekman, D. Daloze, in: *Studies in Natural Products Chemistry* (Ed.: Atta-ur-Rahman), Elsevier, Amsterdam, **1990**, vol. 6, p. 421; c) D. O'Hagan, *Nat. Prod. Rep.* **2000**, *17*, 435–446, and references cited therein; d) J. S. Young, M. A. Kerr, *J. Am. Chem. Soc.* **2007**, *129*, 1465–1469; e) H. U. Kaniskan, P. Garner, *J. Am. Chem. Soc.* **2007**, *129*, 15460–15461.

[2] For some examples, see: a) N.-H. Lin, G. M. Carrera, D. J. Anderson, *J. Med. Chem.* **1994**, *37*, 3542–3553; b) W. M. Kati, D.

Montgomery, R. Carrick, L. Gubareva, C. Maring, K. McDaniel, K. Steffy, A. Molla, F. Hayden, D. Kempf, W. Kohlbrenner, *Antimicrob. Agents Chemother.* **2002**, *46*, 1014–1021; c) J. D. Scott, R. M. Williams, *Chem. Rev.* **2002**, *102*, 1669–1730; d) G. Burton, T. W. Ku, T. J. Carr, T. Kiesow, R. T. Sarisky, J. Lin-Goerke, A. Baker, D. L. Earnshaw, G. A. Hofmann, R. M. Keenan, D. Dhanak, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1553–1556.

[3] a) F. Fache, E. Schultz, M. L. Tommasino, M. Lemaire, *Chem. Rev.* **2000**, *100*, 2159–2231; b) I. Ojiama (Ed.), *Asymmetric Synthesis* 2nd ed., Wiley-VCH, New York, **2000**; c) L. A. Paquette (Ed.), *Chiral Reagents for Asymmetric Synthesis*, Wiley, Chichester, **2003**; d) L. Hoang, S. Bahmanyar, K. N. Houk, B. List, *J. Am. Chem. Soc.* **2003**, *125*, 16–17; e) J. D. White, Q. Xu, C.-S. Lee, F. A. Valeriote, *Org. Biomol. Chem.* **2004**, *2*, 2092–2102; f) C. J. Rogers, T. J. Dickerson, A. P. Brogan, K. D. Janda, *J. Org. Chem.* **2005**, *70*, 3705–3708; g) M. Gruttadauria, R. F. Giacalone, R. Noto, *Chem. Soc. Rev.* **2008**, *37*, 1666–1688.

[4] a) M. Pichon, B. Figadère, *Tetrahedron: Asymmetry* **1996**, *7*, 927–964, and references cited therein; b) A. R. Katritzky, X.-J. Cui, B. Yang, P. J. Steel, *J. Org. Chem.* **1999**, *64*, 1979–1985; c) W. H. Pearson, *Pure Appl. Chem.* **2002**, *74*, 1339–1347; d) M. Besev, L. Engman, *Org. Lett.* **2002**, *4*, 3023–3025; e) C. V. Galliford, M. A. Beenen, S. T. Nguyen, K. A. Scheidt, *Org. Lett.* **2003**, *5*, 3487–3490; f) R. Ballini, G. Bosica, D. Fiorini, A. Palmieri, M. Petrini, *Chem. Rev.* **2005**, *105*, 933–972; g) T. J. Donohoe, G. H. Churchill, K. M. P. Wheelhouse, P. A. Glossop, *Angew. Chem. Int. Ed.* **2006**, *45*, 8025–8028.

[5] Only a few syntheses of 2,3-disubstituted pyrrolidines have been reported, for recent syntheses, see: a) S. Flemer, A. Wurthmann, A. Mamai, J. S. Madalengoitia, *J. Org. Chem.* **2008**, *73*, 7593–7602; b) A. Y. Sukhorukov, A. V. Lesiv, O. L. Eliseev, Y. A. Khomutova, S. M. Ioffe, A. O. Borissova, *Eur. J. Org. Chem.* **2008**, 4025–4034; c) C. Timmons, L. Guo, J. Liu, J. F. Cannon, G. Li, *J. Org. Chem.* **2005**, *70*, 7634–7639.

[6] a) J.-L. Vasse, A. Joosten, C. Denhez, J. Szymoniak, *Org. Lett.* **2005**, *7*, 4887–4889; b) M. Ahari, A. Joosten, J.-L. Vasse, J. Szymoniak, *Synthesis* **2008**, 61–68; c) M. Ahari, A. Perez, C. Menant, J.-L. Vasse, J. Szymoniak, *Org. Lett.* **2008**, *10*, 2473–2476.

[7] This has been anticipated by a preliminary result, already reported in ref.[6b].

[8] a) Y. Yamamoto, N. Asao, *Chem. Rev.* **1993**, *93*, 2207–2293; b) G.-M. Chen, V. Ramachandran, H. C. Brown, *Angew. Chem. Int. Ed.* **1999**, *38*, 825–826; c) S. Itsuno, K. Watanabe, A. A. El-Shehawy, *Adv. Synth. Catal.* **2001**, *343*, 89–94.

[9] High diastereoselectivity has been reported for some simple allylation reactions using In or Zn and imino alcohol chelating aldimines, see: a) R. Yanada, A. Kaieda, Y. Takemoto, *J. Org. Chem.* **2001**, *66*, 7516–7518; b) T. Vilaivan, C. Winotapan, V. Banphavichit, T. Shinada, Y. Ohfune, *J. Org. Chem.* **2005**, *70*, 3464–3471; c) C.-L. K. Lee, H. Y. Ling, T.-P. Loh, *J. Org. Chem.* **2004**, *69*, 7787–7789; d) C.-L. K. Lee, T.-P. Loh, *Org. Lett.* **2005**, *7*, 2965–2967.

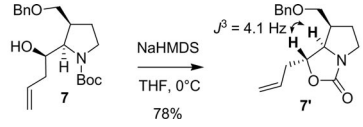
[10] T. Basile, A. Bocoum, D. Savoia, A. Umani-Ronchi, *J. Org. Chem.* **1994**, *59*, 7766–7773.

[11] D. C. Craig, G. L. Edwards, C. A. Muldoon, *Synlett* **1997**, 1441–1443.

[12] S.-H. Kim, S.-I. Kim, S. Lai, J. K. Cha, *J. Org. Chem.* **1999**, *64*, 6771–6775.

[13] Allylation of *N*-CBz-prolinecarbaldehyde using allylindium under Grignard conditions has been described previously, see: I. Izquierdo, M. T. Plaza, V. Yañez, *Tetrahedron: Asymmetry* **2005**, *16*, 3887–3891.

[14] The configuration of the major isomer was deduced from the coupling constant between 7-H and 7a-H in carbamate **7′** obtained by treating **7** with NaHMDS in THF. For assignment of the *cis*/*trans* in prolinol-derived carbamate, see: a) S.-i. Kiyooka, N. Nakano, F. Shiota, R. Fujiyama, *J. Org. Chem.* **1989**, *54*, 5409–5411; b) J. Bejjani, F. Chemla, M. Audouin, *J. Org. Chem.* **2003**, *68*, 9747–9752.



[15] For a racemic synthesis of **10**, see: A. R. de Farias, E. L. Salvador, C. R. D. Correia, *J. Org. Chem.* **2002**, *67*, 3651–3661.

[16] S. L. Buchwald, S. J. La Maire, R. B. Nielsen, B. T. Watson, S. M. King, *Org. Synth.* **1998**, *Coll. Vol. IX*, 162–165.

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