Synthesis and Derivatization of Substituted (*R*)- and (*S*)-*C*-Allylglycines

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Dedicated to Prof. Dr. J. Mulzer on the occasion of his 60th birthday.

Abstract: Various (*R*)- and (*S*)-*C*-allylglycine derivatives were synthesized by means of an auxiliary controlled diastereoselective aza-Claisen rearrangement. Starting from (*S*)-configured auxiliaries derived from optically active proline, an aza-Claisen rearrangement enabled us to synthesize α(*R*)-configured γ,δ-unsaturated amides. Since (*R*)-allylglycine derivatives could be directly generated by reacting *N*-allylproline derivatives and various protected glycine fluorides, the corresponding (*S*)-enantiomers were built-up *via* an initial α-chloroacetyl chloride rearrangement and a subsequent chloride azide substitution with complete inversion of the configuration. High diastereoselectivities were obtained (>15:1). The auxiliary could be efficiently removed by organolithium reactions of the amides furnishing α-amino ketones. Another allyllithium addition allowed us to introduce a second allyl chain with high diastereoselectivity. Final ring closures by means of metatheses using Grubbs' (I) catalyst gave raise to the formation of enantiopure phenanthridines and cyclohexenes displaying defined substitution patterns ready for alkaloid total syntheses.

Keywords: allylation; *C*-allylglycine; aza-Claisen rearrangement; chiral auxiliary; ring closing metathesis

Introduction

(*R*)- and (*S*)-*C*-allylglycine derivatives are widely used in organic synthesis.[1] Because of the high price of the commercially available compound, a set of syntheses had been developed to allow the generation of suitably substituted material for extensive preparative investigations. Generally, the chiral information had been introduced by means of an auxiliary directed strategy.[2]

The ketene aza-Claisen rearrangement (zwitterionic aza-Claisen rearrangement) could be developed as a reliable and flexible reaction to generate various functionalized (*R*)-*C*-allylglycine derivatives with high diastereoselectivity and high yield.[3] Starting from (*S*)-*N*-allylproline methyl ester **1** and *N*-allylprolinol ethers **2** (PG = Bn, TBS), the treatment with diverse protected glycyl fluorides **3** furnished *C*-allylglycine amides **4** and **5**. In all cases, the new stereogenic centre of the major diastereomer **4**/**5** displayed the (*R*)-configuration. The (*S*)-proline methyl ester reactant **1** and acid fluorides **3** bearing small nitrogen substituents (R/R′ = N_3, NPht) resulted in mixtures of diastereomers **4** (predominantly *R*) indicating a non-complete auxiliary directed chiral induction. In contrast, acid fluorides carrying bulky N substituents (R = BOC, CBZ, R′ = Alkyl) gave the desired amides **4** with >15:1 diastereoselectivity in favour of the (*R*)-configured product. However, the rearrangements employing the (*S*)-prolinol derivatives **2** exclusively produced the (*R*)-*C*-allylglycines **5** independently of the nitrogen substituent. Finally, the removal of the chiral auxiliary amide succeeded by means of acid-mediated cleavage, iodolactonization and an aryllithium addition to generate aryl ketones, i.e., isoquinolone **6**, respectively. It should be pointed out that no loss of chiral information had been detected with the removal of the auxiliary (Scheme 1).

In continuation of our program, we report here on the synthesis of further new (*R*)- and (*S*)-*C*-allylglycine derivatives *via* the auxiliary directed strategy. Focussing on the use of the so obtained defined configured amino acid building blocks for heterocycle and carbocycle syntheses, the auxiliary amide moiety of suitably substituted compounds was replaced by means of an organolithium reagent affording optically active γ,δ-unsaturated-α-amino ketones. Then, a stereoselective Grignard addition to the ketone function enabled us to introduce a second unsaturated side chain. Finally, ring closing metatheses allowed us to generate cyclohexenes and phenanthridines displaying a defined substitution pattern. These optically active target compounds should serve

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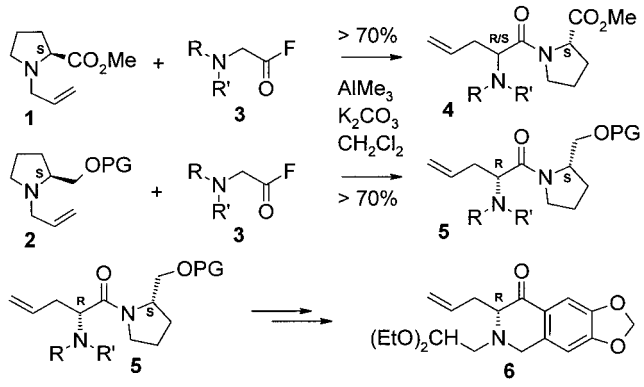
as versatile building blocks in Amaryllidaceae alkaloid total syntheses.

Results and Discussion

Auxiliary Controlled Aza-Claisen Rearrangements

Planning the synthesis of (*S*)-*C*-allylglycine derivatives *via* the auxiliary directed zwitterionic aza-Claisen rearrangement strategy as depicted in Scheme 1, the altered the absolute configuration of the new stereogenic centre had to be taken in account. On one hand, it suggested itself that the change of the auxiliary configuration must enforce the generation of the enantiomeric *C*-allylglycine. The crucial point of such an aim is the significantly higher price of the (*R*)-proline derivatives, preventing the use of the material in bulk quantities. On the other hand, a suitable alternative turned out to be the (*S*)-proline directed introduction of an (*R*)-α-halogen amide and the subsequent substitution of the leaving group by means of nitrogen nucleophile (S_N2).[4] Hence, (*S*)-*N*-allylproline methyl ester and (*S*)-*N*-allylprolinol derivatives and α-chloroacetyl halides were recommended to serve as starting materials. Furthermore, additional allyl systems should be tested to enhance the scope and limitations of the ketene aza-Claisen rearrangement.

Starting from (*S*)-proline methyl ester **7**[5] and (2*S*)-*trans*-4-hydroxyproline methyl ester **8** hydrochloride,[6] respectively, the treatment with allyl bromide **9** and allyl mesylate **10**[7] in the presence of potassium carbonate gave raise to the formation of the *N*-allyl esters **1a** – **c** in 77 to 89% yield.[8] Then, the hydroxy group of ester **1c** was protected as the TBS ether **1d** (98%).[9] The prolinol derivatives **2a**[10] and **2b** were obtained from ester **1a** after DIBALH reduction[11] and the consecutive protection of the newly formed OH group under standard conditions (98–99% yield). The substitution pattern is detailed in Table 1 (Scheme 2).

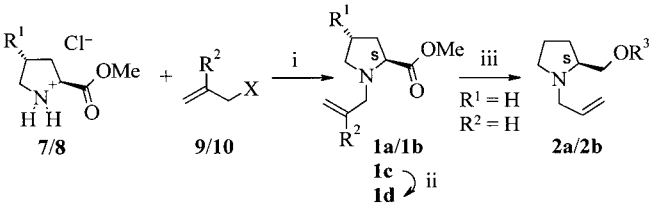


4: d.r. = 1:1 (R,R' = NPht), 4 - 9:1 (R,R' = N_3), >15:1 (R,R' = AlkylNBOC). **5**: d.r. >15:1. PG = Bn, TBS

Scheme 1. Overview: diastereoselective aza-Claisen rearrangements of *N*-allylamines **1** and **2**.

The glycine fluorides **13a** and **13b** had been synthesized *via* four steps starting from 2-aminoacetaldehyde dimethyl acetal **11a** and bromopiperonylamine **11b**.[12] The amines **11** were alkylated with ethyl bromoacetate to give the intermediate glycine esters. Then, the nitrogen was protected as a *t*-butyl carbamate. After basic aqueous cleavage of the ester function, the corresponding carboxylic acids **12a** and **12b** could be isolated with high yield (66–93% over three steps). Finally, the reaction with cyanuric fluoride under standard conditions afforded the acid fluorides **13a** and **13b** (94.5–99.5%).[13] The so activated acid derivatives were used as crude compounds. No extensive purification was necessary to obtain satisfactory reactive material. Additionally, chloroacetyl chloride **13c** and azidoacetyl fluoride **13d** were used as reactants in diverse ketene aza-Claisen rearrangements[13] (Scheme 3).

First zwitterionic aza-Claisen rearrangements were conducted with the *N*-allylproline methyl esters **1a** – **d** and acid halides **13c** and **13d**. Focussing on the synthesis of (*S*)-*C*-allylglycine, the *N*-allylamino ester **1a** was treated with chloroacetyl chloride **13c** to give the α-chloroamide **14a** in 70% yield as a single diastereomer. As expected, the formation of the desired amide **14a** was accompanied by the generation of some von Braun degradation products (allyl chloride and *N*-chloroacetylpyrrolidide of **7**),[14] pointing out the efficiency of

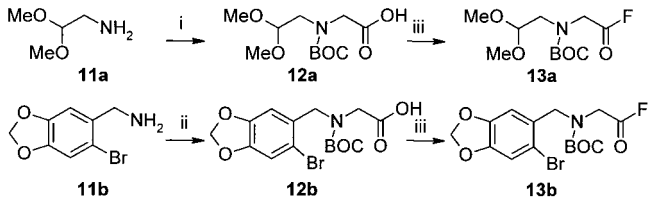


i) K_2CO_3, DMF, rt, 20 h (**1a**: 89%, **1b**: 77%, **1c**: 81.5%). ii) TBSCl, DMAP cat., imidazole, THF, 20 h, 0 °C - rt (98%). iii) 1. DIBALH, THF, 0 °C, 3 h; 2. TBSCl, DMAP cat., imidazole, THF, rt, 3 h (**2a**: 98%) and TPSCl, DMAP cat., imidazole, THF, rt, 3 h (**2b**: 99%). For substitution pattern see Table 1.

Scheme 2. Syntheses of optically active *N* allylpyrrolidines.

Table 1. Substitution patterns of the allylamines

No.	R^1	R^2	R^3	X
1a	H	H	–	–
1b	H	CH_2OTBS	–	–
1c	OH	H	–	–
1d	OTBS	H	–	–
2a	H	H	TBS	–
2b	H	H	TPS	–
7	H	–	–	–
8	OH	–	–	–
9	–	H	–	Br
10	–	CH_2OTBS	–	OMes



i) 1. $BrCH_2CO_2Et$, Et_3N, Et_2O, 0 °C, 20 h. 2. BOC_2O, Et_2O, 5 h, rt. 3. 1 M aq. NaOH, LiCl, 3 h, rt (66%). ii) 1. $BrCH_2CO_2Et$, Et_3N, THF, 0 °C, 20 h. 2. BOC_2O, THF, 5 h, rt. 3. 0.1 M aq. NaOH, LiCl, 80 °C (93%). iii) $(CFN)_3$, Py, CH_2Cl_2, 0 °C, 1.5 h (**13a**: 94.5%, **13b**: 99.5%)

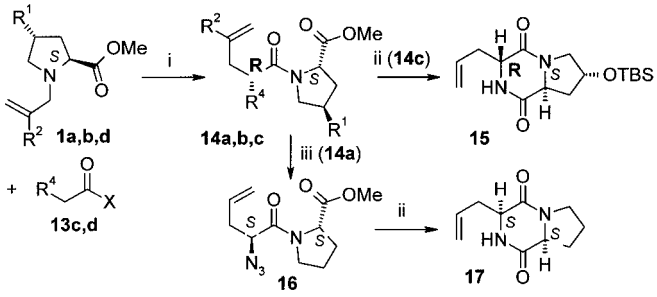
Scheme 3. Syntheses of glycyl fluorides.

this competing reaction even in the presence of the highly rearrangement-active starting material. However, the decrease of the yield was acceptable ($<10\%$). A further optimization would have been achieved using chloroacetyl fluoride. The (2*R*)-chloroamide **14a** was then subjected to a nucleophilic substitution (S_N2). The reaction with sodium azide in DMF afforded the (2*S*)-azidoamide **16** in nearly quantitative yield.[4] The spectral data of the (*S*)-*C*-allylglycine derivative displayed significant differences to that obtained for the corresponding (*R*)-material. Finally, the Staudinger reaction[12c] and the aqueous work-up of the phosphine imine induced the immediate cyclization of the new amino group and the auxiliary ester function. The piperazinedione **17** was isolated in 91% yield. The relative configuration of the stereogenic centres could be unequivocally proven by means of NOESY analysis, the new centre of the *C*-allylglycine moiety selectively exhibited the (*S*)-configuration (Figure 1; Scheme 4).

The reactions of the allylamino esters **1b** and **1d** with azidoacetyl fluoride produced the (2*R*)-azidoamides **14b** and **14c** with 75 and 79% yield, respectively. According to extensive spectroscopic and HPLC analyses, both rearrangements were found to be diastereoselective, pointing out the highly simple and highly auxiliary directed asymmetric induction. In analogy to the (2*S*)-experiment mentioned above, the amide **14c** was subjected to the Staudinger reaction and aqueous work-up of the phosphine imine. The immediate cyclization of the new amino group and the auxiliary ester function furnished the piperazinedione **15** in 85% yield. The relative configuration of the stereogenic centres could be unequivocally proven by means of NOESY analysis, the new centre of the *C*-allylglycine moiety selectively displayed the (*R*)-configuration (d.r. $>20:1$, Figure 1; Scheme 4).

Although the ester auxiliary directed rearrangements described above were characterized by high yields and high asymmetric induction, the methyl ester function of the proline moiety prevented any Grignard type removal of the amide. The envisaged organolithium reactions (like **5** → **6**, Scheme 1) required the absence of any additional reactive carbonyl and carboxyl functions.

Figure 1. NOESY analyses of piperazinediones **15** and **17**. Significant correlations are marked with arrows, pivotal effects are marked with "**!**".



i) Me_3Al, K_2CO_3, CH_2Cl_2, –20 °C, 1 h or 0 °C, 3 h (**14a**: 70%, **14b**: 79%, **14c**: 75%). ii) PPh_3, THF, H_2O, 16 h, rt (**15**: 85%, **17**: 91%). iii) NaN_3, DMF, 20 h, rt (97%). For substitution pattern see Table 2.

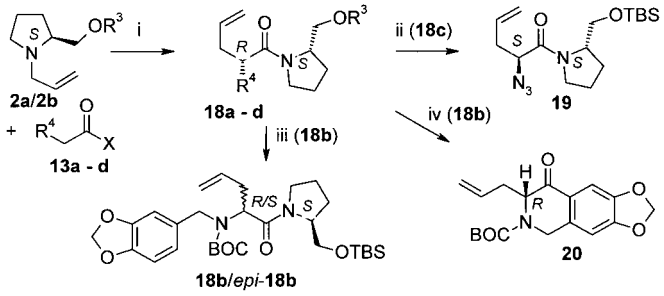
Scheme 4. Methyl ester auxiliary-directed aza-Claisen rearrangements.

Consequentially, the (*S*)-prolinol derivatives **2a**/**b** were used as chiral allylation compounds. The treatment of TPS-prolinol **2b** with azidoacetyl fluoride **13d** (X = F) under standard conditions afforded the amide **18d** (R^3 = TPS, $R^4 = N_3$) in 76% yield as a single diastereomer.[15] The intermolecular rearrangement involving chloroacetyl chloride **13c** (X = Cl) and allylamine **2a** (R^3 = TBS) selectively gave the corresponding (α*R*)-chloroamide **18c** in 69% yield (d.r. $>20:1$). Again, some degradation products (allyl chloride, chloroacetylprolinol amide) were formed during the course of the process pointing out the superiority of the acyl fluoride-mediated rearrangements. The substitution of the chloride in **18c** by means of sodium azide in DMF gave the (2*S*)-configured α-azidoamide **19** in 99% yield. In analogy to previous experiments, the reaction of allylamine **2a** (R^3 = TBS) and the fluorides **13a** and **13b** smoothly gave the C-allylglycine derivatives **18a** (72%) and **18b** (82%). As expected, a single diastereomer had been formed, respectively, according extensive spectral and HPLC analyses. The generation of a mixture of diastereomers could be enforced upon refluxing the pure *C*-allylglycine derivative **18b** in DMF in the presence of potassium carbonate. After about 20 h a second compound **18b**-*epi* occurred, which could be separated by means of HPLC (56% of **18b**, 36% of **18b**-*epi*). All spectral and analytical data supported the formation of a diastereomer of **18b**.[16] Consequentially; the rearrangement building-up the amides **18a–d** must have been diastereoselective. The removal of the chiral auxiliary of amide

18b proceeded with moderate 41.5% yield resulting isoquinolizidinone **20**.[17] Obviously, the treatment of **18b** with *n*-BuLi induced the bromine-lithium exchange. The so formed aryllithium moiety suffered from two competing reactions: the first part delivered the desired ketone **20** attacking the amide function. A second part of the lithium reagent might have attacked the BOC carbonyl function in terms of a 5-*exo-trig* process removing the protecting group. Consecutive processes destroyed this part of the material resulting in the relatively low yield of the conversion. The substitution pattern of the amides is detailed in Table 2 (Scheme 5).

The analysis of the stereochemical outcome of all ketene aza-Claisen rearrangements was found to be in strong accordance with that published earlier supporting the given working hypothesis.[3] Thus, only a brief summary of the mechanistic discussion will be outlined here.[18]

The reaction path of the auxiliary controlled intermolecular rearrangement was thought to start with the addition of the Lewis acid activated ketene moiety **13*** (derived from acid halide **13** and Me_3Al, methane evolution) to the allylamines **1** and **2**, respectively. Presuming a favored amine conformation with minimized repulsive interactions, especially bulky ketene equivalents **13*** should attack the lone pair in the favored arrangement **2*** to generate diastereoselectively the *syn*-allylammonium enolate. The so formed zwitterion was characterized by a (*Z*)-enolate geometry as known for related systems.[19] Finally, the allylammonium enolate underwent the 3,3 sigmatropic conversion, the charge neutralization should serve as a highly efficient driving force. In accordance to well known Claisen rearrangements, a chair-like transition state should be involved minimizing 1,3 repulsive interactions.[20] Consequentially, the small CH_2 part of the auxiliary must have been placed quasi-axial, the bulky chain branched centre must have been arranged in the quasi-equatorial position. Overall, the (*S*)-configuration of the auxiliary centre caused the diastereoselective formation of the (αR)-configuration in the newly formed amide (Figure 2, for allyl ester **1a – d** replace CH_2OR^3 of **2a/b** by CO_2Me).



Scheme 5. Prolinol auxiliary directed aza-Claisen rearrangements.

Synthesis of Phenanthridines and Cyclohexenes

The amides **5**, **14**, **16**, **18** and **19** represent useful starting materials for further synthetic investigations. The gener-

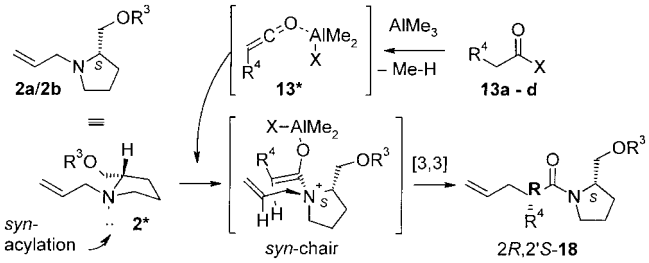


Figure 2. Stereochemical rationalization of the auxiliary controlled aza-Claisen rearrangement: working hypothesis.

Table 2. Substitution patterns of the acid halides **13** and the γ,δ unsaturated amides **14** – **19**.

No.	R^1	R^2	R^3	R^4
13a	–	–	–	$(MeO)_2CHCH_2$-N-BOC
13b	–	–	–	3,4-methylenedioxy-6-bromobenzyl-N-BOC
13c*	–	–	–	Cl
13d	–	–	–	N_3
14a	H	H	Ester	Cl
14b	H	CH_2OTBS	Ester	N_3
14c	OTBS	H	Ester	N_3
16	H	H	Ester	N_3
18a	H	H	TBS	$(MeO)_2CHCH_2$-N-BOC
18b	H	H	TBS	3,4-methylenedioxy-6-bromobenzyl-N-BOC
18c*	H	H	TBS	Cl
18d	H	H	TPS	N_3
19	H	H	TBS	N_3

13: X = F except *: X = Cl.

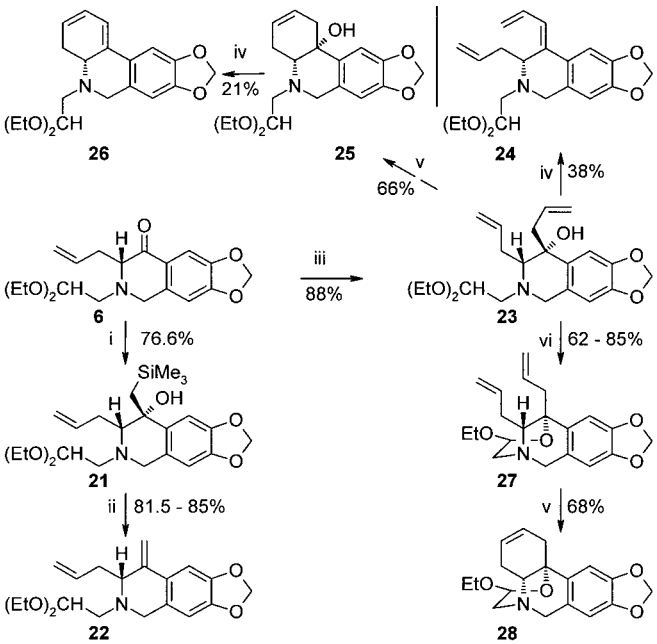
ation of optically active isoquinolones **6** and **20** *via* intramolecular Grignard-type cyclization enabled us to remove the chiral auxiliary in a highly efficient manner.[3,17] Starting from isoquinolone **6**, the keto function should be converted into an exocyclic olefin intending to prepare the material for another ring annulation. Several attempts using Wittig- and Horner-type olefinations failed in spite of a broad variation of the reagents and the reaction conditions. Finally, the introduction of an exomethylene group succeeded using a Peterson protocol.[21] Initially, trimethylsilylmethyllithium[22] was added to isoquinolone **6** to give carbinol **21** in 76.6% yield as a single diastereomer.[23] A NOESY analysis proved the *syn*-configuration of the hydroxy group and the allyl side chain (Figure 3). Then, β-elimination of OH and TMS functions could be achieved under basic (NaH, THF, 81.5%)[24] and acidic conditions (AcOH, $CHCl_3$, 85%),[25] respectively, generating the isoquinoline **22**. It was noteworthy that no cleavage of the diethyl acetal was observed. Obviously, the basic isoquinoline nitrogen trapped all protons before affecting the acetal moiety (Scheme 6).

The success of the diastereoselective lithium organyl addition to isoquinolone **6** mentioned above motivated us to investigate a further reagent. Allyllithium had been generated by a transmetallation of allyltributyltin and butyllithium.[26] The reaction with ketone **6** delivered the vicinal diallylquinoline **23** in 88% yield as a single diastereomer. Again, the *syn*-arrangement of the OH group and the adjacent allyl side chain could be proven by means of a NOESY analysis.[27] First attempts to enforce the β-elimination of H_2O had been conducted under basic conditions. Treatment of carbinol **23** with MsCl in the presence of *t*-BuOK gave the butadiene **24** in 38% yield. The newly formed double bond selectively displayed the (*Z*) geometry. Unfortunately the diene tended to decompose easily preventing extensive subsequent experiments (Scheme 6).

Olefin metathesis is known as a powerful reaction to close 6-membered rings.[28] Planning to involve such a process to generate phenanthridine **25** from the vicinal diallyl quinoline **23**, an electron-rich nitrogen centre (as present in **23**) was known to interfere with a smooth metathesis because of the effective complexation of the catalyst metal centre. As expected, the RCM of diallylquinoline **23** was found to be very slow but the ring closure could be enforced by refluxing in $CHCl_3$ for 4 days in the presence of Grubbs (I) catalyst (benzylidenebis-[dicyclohexylphosphine] ruthenium dichloride). Complete conversion of the starting material could be achieved by adding 5 mol % portions of the catalyst every 24 h, overall 20 mol % of the ruthenium complex were needed. Finally, the phenanthridine **25** could be isolated in 66% yield. Again, the β-elimination of H_2O was found to be difficult. Treatment of carbinol **25** with MsCl in the presence of *t*-BuOK gave the cyclohexadiene **26** in 21% yield. The phenanthridine **26** was unstable upon column chromatography and upon storing even at −20 °C (Scheme 6).[29]

Upon treating the diallylquinoline **23** with aqueous HCl[30] and $CeCl_3$/AcCl[31] in $CHCl_3$, no β-elimination of H_2O had been observed. In contrast, a transacetalization gave raise to the formation of isoquinoline **27** in 62% (HCl) and 85% ($CeCl_3$) yields. Prolonged reaction times and increased acid concentrations did not cause the complete cleavage of the remaining ethoxy function. Obviously, the basic isoquinoline nitrogen prevented an efficient acetal cleavage by an effective trapping of proton and Lewis acid, respectively. However, isoquinoline **27** had been subjected to the RCM conditions as outlined for the phenanthridine **25** synthesis. Analogously, the corresponding ring closure afforded the phenanthridine **28** in 68% yield. Again, the RCM was very slow and 20 mol % ruthenium reagent were necessary to obtain a complete consumption of the reactant **27** (complexation ability of the electron-rich nitrogen centre) (Scheme 6).

Starting from amide **18a**, the removal of the auxiliary pyrrolidine by means of an intermolecular lithium organyl addition had been investigated. The reaction of amide **18a** and piperonyllithium under standard conditions resulted ketone **29** in 67.5% yield. The absence of racemization has been demonstrated satisfactorily (chiral HPLC, NMR). The α-aminoketone **29** was then treated with allyllithium to give the diallylamino alcohol **30** in almost quantitative yield as a single diastereomer.



i) $TMSCH_2Li$, THF, –78 °C, 3 h. ii) NaH, THF, 0 °C/1 h and reflux/3 h or AcOH, $CHCl_3$, rt, 3 h. iii) allyl-Li, –78 °C/1 h and –60°C/1 h. iv) MsCl, KO*t*Bu, DMSO, rt, 2 d. v) 20% Grubbs I catalyst, $CHCl_3$, 60 °C, 4 d. vi) 1 M aq. HCl, 50°C, 20 h or $SmCl_3$, AcCl, rt, 30 min.

Scheme 6. Syntheses of optically active isoquinolines and phenanthridines.

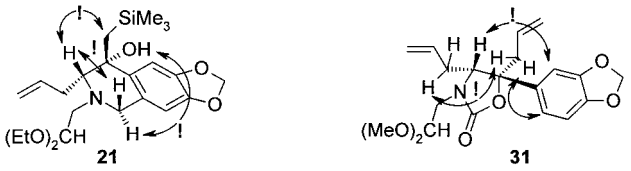
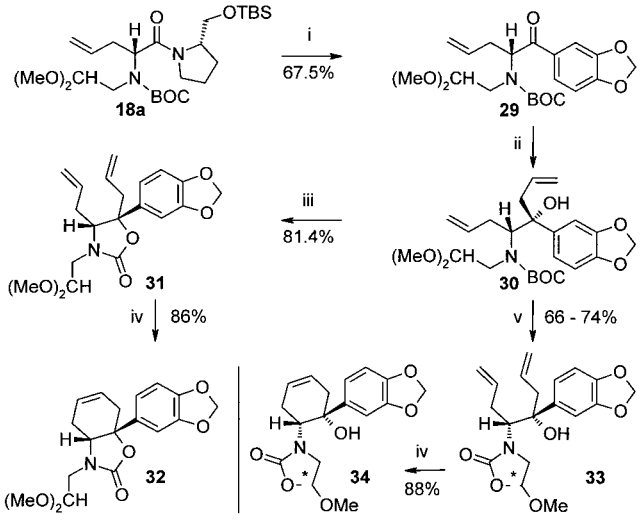


Figure 3. NOESY Analyses of allyl adducts **21** and **31**. Significant correlations are marked with arrows, pivotal effects are marked with"**!**".

The so obtained crude material was used without further purification. Surprisingly, treatment of carbinol **30** with KHMDS in THF at 0 °C led to a smooth cyclization to give carbamate **31** in 86% yield. Obviously, the 5-*exo-trig* situation of the intermediate alcoholate and the BOC carbonyl function enabled us to remove the *tert*-butyl alcohol under basic conditions (transesterification). An NOESY analysis proved the *cis*-configuration of the allyl side chains in **31** (Figure 3, *vide supra*) pointing out the diastereoselective allylation of the ketone **29**. A final RCM process afforded the cyclohexene **32** in 86% yield. The less electron-rich nitrogen centre allowed us to conduct the metathesis under well known conditions: only 5 mol % Grubbs (I) catalyst were necessary to achieve complete consumption of the reactant **31** within 3 h at 60 °C (Scheme 7).

Treatment of carbinol **30** with $CeCl_3$/AcCl in $CHCl_3$ and with wet DMSO at 80–90 °C[32] induced a transacetalization to give the carbamate **33** as a mixture of two diastereomers (not separated). The final RCM afforded the cyclohexenes **34** in 88% yield. Again, the less electron-rich nitrogen centre allowed us to conduct the metathesis under well known conditions: only 5 mol % Grubbs (I) catalyst were necessary to achieve complete consumption of the reactant **31** within 3 h at 60 °C. Overall, the RCM strategy enabled us to synthesize optically active phenanthridines and cyclohexenes , respectively, displaying suitable substitution patterns for further investigations (Scheme 7).



i) piperonyl-Li, THF, –78 °C, 30min. ii) allyl-Li, –78 °C/1 h and –60 °C/1 h. iii) KHMDS, THF, 0 °C, 30 min. iv) 5% Grubbs I catalyst, $CHCl_3$, 60 °C, 3 h. v) cat. $SmCl_3$, AcCl, rt, 30 min or DMSO, H_2O, 80 - 90 °C, 20 h.

Scheme 7. Syntheses of optically active cyclohexenes.

Conclusion

(*R*)- and (*S*)-*C*-allylglycine derivatives have been synthesized using an auxiliary directed α-*C*-allylation of glycine and chloroacetyl halides. Always the (*S*)-configured auxiliary pyrrolidine substituent derived from L-proline caused the formation of (α*R*)-γ,δ-unsaturated amides with high diastereoselectivity using a zwitterionic aza-Claisen rearrangement as the key step. Various (*R*)-*C*-allylglycines have been obtained directly *via* the reaction of *N*-protected glycyl fluorides and *N*-allylpyrrolidines. In contrast, the (*S*)-*C*-allylglycine synthesis required one intermediate step when intending to use the same (*S*)-configured auxiliary series. Initially, chloroacetyl chloride and the allylamine were combined to give the (α*R*)-chloroamide, which underwent a smooth substitution with azide to give the (α*S*)-azidoamides with complete inversion of the configuration. As expected, the employment of carboxylic acid chlorides caused some von Braun degradation within the reaction, pointing out the superiority of the acyl fluorides as key compounds in ketene aza Claisen rearrangements. The auxiliary moiety of the γ,δ-unsaturated amides could be removed by conducting a C–C bond forming step. Treatment with organolithium compounds gave raise to the formation of (α*R*)-amino ketones.

Since direct olefinations of the aryl ketones gave no satisfactory results, another organolithium addition to the ketone function enabled us to introduce a new side chain with high 1,2 asymmetric induction. Subsequent elimination allowed us to generate defined olefins. Focussing on the formation of new ring systems, 1,2-diallyl compounds were subjected to RCM conditions. The isoquinoline derivatives bearing an electron-rich (basic) nitrogen required long reaction times and high catalyst concentrations to achieve the formation of phenanthridines in > 65% yield. In contrast, the carbamate-protected open chain amino alcohols furnished cyclohexenes with 5% catalyst in short times with > 80% yield. The so formed compounds represent suitable precursors for Amaryllidaceae alkaloid total syntheses.

Experimental Section

General Remarks

^{1}H NMR, ^{13}C NMR spectra and NOESY experiments were recorded on Bruker AC 250 or on a Bruker AC 550 spectrometer

at room temperature unless specified otherwise. Tetramethylsilane was used as internal standard. IR spectra were obtained from a Perkin Elmer 257 or 580B spectrophotometer. Optical rotations were measured with a Perkin Elmer P 241 polarimeter in a 1 dm cell. Mass spectra were recorded on a Varian MAT 711 or 112S, The high resolution mass spectra (HRMS) were obtained with a Varian MAT 711 spectrometer. PFK was used as reference, the results were determined *via* a peak matching method, resolution: > 10000. Ion source temperature was 250 °C, electron energy was 0.8 mA. The melting points (not corrected) were measured with a Büchi SMP 20. For HPLC, Knaur pumps, UV-and RI detectors, and Rheodyne injection systems were used. Preparative amounts of several compounds were separated with a 32 mm × 250 mm column and 5 μm Nucleosil 50–5 obtained from Macherey & Nagel, with a flow of about 80 mL/min. Chiral HPLC analyses were run using Chirobiotic-V and Chirobiotic-T columns (Baker). Column chromatography was carried out with Merck silica gel 0.063–0.2 mm, 70–230 mesh A. The progress of the reactions was monitored by thin layer chromatography (TLC) performed on aluminium sheets pre-coated with silica gel 60 (thickness 0.25 mm). All solvents were dried before use following standard procedures.

(*S*)-*N*-(2-*tert*-Butyldimethylsilyloxymethyl) 2-propenylproline Methyl Ester (1b)

Proline methyl ester hydrochloride (**7**; 1.14 g, 6.90 mmol) in DMF (100 mL) was treated with Et_3N (1.3 g, 6.90 mmol) and mesylate **10** (1.61 g, 5.75 mmol) at 0 °C. The mixture was stirred overnight at 20 °C, then H_2O (50 mL) was added. The aqueous layer was extracted with Et_2O (4 × 20 mL), the combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude material was purified by column chromatography (*n*-hexane/ethyl acetate = 5:1) to give *N*-allylproline methyl ester **1b** as pale yellow oil; yield: 1.4 g (77%); $[\alpha]_D^{20}$: −51.7° (*c* 1.7, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.05 [s, 6H, Si(C*H*$_3$)$_2$], 0.90 [s, 9H, SiC(C*H*$_3$)$_3$], 1.65–1.97 (m, 3H, C*H*$_2$CH*H*), 1.99–2.15 (m, 1H, CH$_2$C*H*H), 2.26–2.38 (dd, 1H, *J* = 16.60 Hz, 8.30 Hz, NCH*H*CH$_2$), 2.96–3.07 (m, 2H, NC*H*HCH$_2$, NCH*H*CH=CH$_2$), 3.11–3.18 (dd, 1H, *J* = 8.79 Hz, 5.37 Hz, NC*H*CO$_2$), 3.20–3.28 (d, 1H, *J* = 12.70 Hz, NC*H*HCH=CH$_2$), 3.65 (s, 3H, CO$_2$C*H*$_3$), 4.07–4.25 (dd, 2H, *J* = 21.49 Hz, 14.65 Hz, TBSOC*H*$_2$), 4.95 (s, 1H, CH*H*=C), 5.05 (s, 1H, C*H*H=C) ppm; ^{13}C NMR (68 MHz, $CDCl_3$): δ = −5.4 [Si(*C*H$_3$)$_2$], 18.3 [Si*C*(CH$_3$)$_3$], 23.0 (*C*H$_2$CH$_2$), 25.8 [SiC(*C*H$_3$)$_3$], 29.3 (CH$_2$*C*H$_2$), 51.5 (O*C*H$_3$), 53.3 (N*C*HCO$_2$), 57.5 (N*C*H$_2$CH$_2$), 64.4 (N*C*H$_2$C=CH$_2$), 65.4 (TBSO*C*H$_2$), 111.3 (*C*H$_2$=C), 146.2 (CH$_2$=*C*), 174.6 (*C*O$_2$CH$_3$); IR (KBr, film): 1/λ = 3092 (w), 2954 (s), 2929 (s), 2884 (m), 2856 (s), 1752 (s, COO), 1737 (s, COO), 1658 (w), 1472 (m), 1462 (m), 1435 (m), 1406 (w), 1388 (w), 1361 (m), 1251 (s), 1196 (s), 1171 (s), 1108 (s), 1040 (w), 1006 (m), 938 (w), 906 (m) cm^{-1}; MS (EI, 80 eV, 40 °C): *m/z* (%) = 313 (3, [M]$^+$), 298 (3, [M − CH$_3$]$^+$), 254 (100, [M − CO$_2$CH$_3$]$^+$), 185 (19, [M − C$_6$H$_{10}$NO$_2$]$^+$), 128 (33, [M − C$_6$H$_{11}$NO$_2$ − C$_4$H$_9$]$^+$); HRMS (80 eV, 40 °C): calcd. for $C_{16}H_{31}NO_3Si$: 313.20732; found: 313.20722.

(2*S*,4*R*)-*N*-Allyl-4-hydroxyproline Methyl Ester (1c)

To a suspension of hydroxyproline methyl ester **8** (2 g, 11 mmol) in dry CH_2Cl_2 (50 mL) was added Et_3N (1.56 mL) and freshly distilled allyl bromide **9** (1.12 mL, 13.2 mmol, *d* = 1.43). The mixture was stirred overnight at 20 °C. Then H_2O (30 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL), the combined organic layers were dried over $MgSO_4$, and the solvent was removed under vacuum. The crude material was purified by column chromatography (ethyl acetate) to give allylhydroxyproline methyl ester **1c** as pale yellow oil; yield: 1.66 g (81.5%); $[\alpha]_D^{20}$: −87.3° (*c* 1.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.90–1.98 (m, 1H, HOCHC*H*$_2$), 2.01–2.09 (m, 1H, HOCHC*H*$_2$), 2.29–2.35 (ddd, 1H, *J* = 9.90 Hz, 5.45 Hz, 4.45 Hz, NCH*H*), 3.01–3.07 (m, 1H, CH*H*CH=CH$_2$), 3.17–3.23 (m, 1H, C*H*HCH=CH$_2$), 3.23–3.29 (ddd, 1H, *J* = 10.40 Hz, 5.45 Hz, 4.95 Hz, NC*H*H), 3.34–3.40 (m, 1H, NC*H*), 3.43–3.55 (br, s, OH), 3.55 (s, OCH$_3$), 4.96–5.01 (dd, 1H, *J* = 10.03 Hz, 0.98 Hz, CH=CH*H*),), 5.03–5.09 (dd, 1H, *J* = 17.05 Hz, 1.24 Hz, CH=C*H*H), 5.70–5.80 (m, 1H, C*H*=CH$_2$) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 39.3 (HOCH*C*H$_2$), 51.6 (O*C*H$_3$), 57.1 (*C*H$_2$CH=CH$_2$), 61.0 (N*C*H$_2$), 63.4 (N*C*HCOOCH$_3$), 69.3 (*C*HOH), 117.6 (CH=*C*H$_2$), 134.4 (*C*H=CH$_2$), 173.9 (*C*OO); IR (KBr, film): 1/λ = 3173 (br, m, OH), 3072 (m), 3024 (m), 3007 (m), 2985 (m), 2975 (m), 2953 (m), 2945 (m), 2866 (m), 2823 (m), 1878 (w), 1747 (s, COO), 1706 (w), 1644 (w), 1462 (m), 1453 (m), 1432 (m), 1377 (m), 1364 (w), 1340 (m), 1320 (m), 1287 (w), 1266 (w), 1235 (m), 1218 (m), 1196 (s), 1174 (s), 1142 (m), 1127 (m), 1091 (s), 1061 (w), 1019 (m) cm^{-1}; MS (EI, 80 eV, 30 °C): *m/z* (%) = 185 (7.4, [M]$^+$), 126 (100, [M − C$_2$H$_3$O$_2$]$^+$), 108 (7, [M − C$_2$H$_5$O$_3$]$^+$), 41 (19, [C$_3$H$_5$]$^+$); HRMS (80 eV, 30 °C): calcd. for $C_9H_{15}NO_3$: 185.10519; found: 185.10733.

(2*S*,4*R*)-*N*-Allyl-4-*tert*-butyldimethylsilyloxyproline Methyl Ester (1d)

N-Allylhydroxyproline methyl ester (**1c**; 1.4 g, 7.57 mmol), imidazole (1.13 g, 16.6 mmol) and DMAP (10 mg) in anhydrous THF (20 mL) were treated with TBSCl (2.28 g, 15.14 mmol) at 0 °C. After 3 hours of stirring at 20 °C (TLC control), the mixture was quenched with MeOH (20 mL) and H_2O (20 mL). The aqueous layer was extracted with Et_2O (4 × 10 mL) and the combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude material was purified by column chromatography (hexane-EtOAc, 5:1) to give silyl ether **1d** as pale yellow oil; yield: 2.2 g (98%); $[\alpha]_D^{20}$: −47.8° (*c* 1.5, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.00 [s, 6H, Si(C*H*$_3$)$_2$], 1.35 [s, 9H, SiC(C*H*$_3$)$_3$], 1.87–1.99 (ddd, 1H, *J* = 12.69 Hz, 8.30 Hz, 3.91 Hz, NCHCH*H*), 1.99 (ddd, 1H, *J* = 12.70 Hz, 7.81 Hz, 7.25 Hz, NCHC*H*H), 2.24–2.32 (dd, 1H, *J* = 9.76 Hz, 6.88 Hz, NCH*H*CHO), 3.00–3.11 (dd, 1H, *J* = 13.19 Hz, 7.33 Hz, CH*H*CH=CH$_2$), 3.19–3.30 (m, 2H, NC*H*HCHO, C*H*HCH=CH$_2$), 3.31–3.39 (dd, 1H, *J* = 8.30 Hz, 7.81 Hz, NC*H*), 3.65 (s, 3H, OC*H*$_3$), 4.27–4.37 (m, 1H, TBSOC*H*), 4.97–5.09 (dd, 1H, *J* = 9.76 Hz, 0.98 Hz, CH=CH*H*), 5.09–5.15 (dd, *J* = 17.09 Hz, 1.47 Hz, CH=C*H*H), H), 5.71–5.88 (dddd, 1H, *J* = 17.09 Hz, 10.25 Hz, 9.76 Hz, 6.83 Hz, C*H*=CH$_2$); ^{13}C NMR (68 MHz, $CDCl_3$): δ = −5.0 [Si(*C*H$_3$)$_2$], 17.8 [Si*C*(CH$_3$)$_3$], 25.6 [SiC(*C*H$_3$)$_3$], 39.6 (OCH*C*H$_2$), 51.7 (O*C*H$_3$), 58.1 (N*C*H$_2$CH=CH$_2$), 61.6 (N*C*H$_2$), 64.0 (N*C*HCOOCH$_3$), 70.3 (O*C*HCH$_2$), 117.6

(CH=CH_2), 134.8 (*C*H=CH_2), 174.2 (*C*O); IR (KBr, film): 1/λ = 3079 (w), 2954 (s), 2929 (s), 2896 (m), 2857 (s), 2803 (m), 2710 (w), 1751 (s, CO), 1659 (w), 1643 (w), 1472 (m), 1463 (m), 1436 (m), 1420 (w), 1361 (m), 1312 (w), 1257 (s), 1198 (s), 1173 (s), 1131 (m), 1099 (s), 1033 (m), 1006 (m), 995 (m) cm^{-1}; MS (EI, 80 eV, 40 °C): *m/z* (%) = 299 (3, $[M]^+$), 284 (2, $[M - CH_3]^+$), 240 (100, $[M - C_2H_3O_2]^+$); HRMS (80 eV, 40 °C): calcd. for $C_{15}H_{29}NO_3Si$: 299.19167; found: 299.19192.

(*S*)-*N*-Allyl-2-*tert*-butyldiphenylsilyloxymethylpyrrolidine (2b)

(*S*)-*N*-Allylprolinol (1 g, 7.08 mmol; prepared and characterized as reported[10]), imidazole (1 g, 14.7 mmol) and DMAP (10 mg) in anhydrous THF (50 mL) were treated with TPSCl (2.9 g, 10.5 mmol) at 0 °C. After 3 hours of stirring at 20 °C (TLC control), the mixture was quenched with H_2O (20 mL). The aqueous layer was extracted with Et_2O (4 × 10 mL) and the combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude material was purified by column chromatography (*n*-hexane/ethyl acetate, 4:1) to give TPS-prolinol **2b** as a colourless oil; yield: 2.68 g (99%); $[\alpha]_D^{20}$: −46.2° (*c* 1.9, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.10 [s, 9H, SiC(C*H*$_3$)$_3$], 1.60–1.85 (m, 3H, C*H*$_2$CH*H*), 1.85–2.01 (m, 1H, CH$_2$C*H*H), 2.20–2.31 (m, 1H, NCH*H*CH$_2$), 2.62–2.74 (m, 1H, NC*H*CH$_2$O), 2.89–2.99 (dd, 1H, *J* = 13.18 Hz, 7.32 Hz, NCH*H*CH=CH$_2$), 3.03–3.11 (m, 1H, NC*H*HCH$_2$), 3.47–3.56 (m, 1H, NC*H*HCH$_2$), 3.49–3.58 (dd, 1H, *J* = 10.25 Hz, 6.84 Hz, CH*H*OTPS), 3.73–3.81 (dd, 1H, *J* = 10.26 Hz, 6.36 Hz, C*H*HOTPS), 5.01–5.08 (dd, 1H, *J* = 10.26 Hz, 0.98 Hz, CH=CH*H*), 5.09–5.19 (dd, 1H, *J* = 17.09 Hz, 1.46 Hz, CH=C*H*H), 5.79–5.96 (dddd, 1H, *J* = 17.09 Hz, 10.25 Hz, 7.32 Hz, 5.86 Hz, C*H*=CH$_2$), 7.30–7.55 (m, 5H, Ph), 7.65–7.82 (m, 3H, Ph). ^{13}C NMR (68 MHz, $CDCl_3$): δ = 19.1 [Si*C*(CH$_3$)$_3$], 22.8 (*C*H$_2$CH$_2$), 26.8 [SiC(*C*H$_3$)$_3$], 28.4 (CH$_2$*C*H$_2$), 54.4 (N*C*H$_2$CH=CH$_2$), 58.5 (N*C*H$_2$CH$_2$), 64.6 (N*C*HCH$_2$O), 67.5 (NCH*C*H$_2$O), 116.4 (CH=*C*H$_2$), 127.5, 129.4, 133.7, 136.2 (Ph), 135.5 (*C*H=CH$_2$); IR ($CHCl_3$): 1/λ = 3072 (m), 3045 (m), 2807 (m), 3017 (s), 2964 (s), 2931 (s), 2859 (s), 2807 (m), 1472 (m), 1463 (w), 1428 (m), 1391 (w), 1215 (s), 1112 (s), 1050 (m) cm^{-1}; MS (EI, 80 eV, 40 °C): *m/z* (%) = 379 (5, $[M]^+$), 322 (6, $[M - C_4H_9]^+$), 280 (4, $[M - C_4H_9 - C_3H_6]^+$), 199 (43, $[HOSiPh_2]^+$), 110 (100, $[C_7H_{12}N]^+$); HRMS (80 eV, 30–40 °C): calcd. for $C_{24}H_{33}NOSi$: 379.23314; found: 379.23454.

N-*tert*-Butyloxycarbonyl-N-(2,2-dimethoxyethyl)aminoacetic Acid (12a)

Aminoacetaldehyde dimethyl acetal (**11a**; 4.60 g, 43.8 mmol) and Et_3N (44.2 g, 61.3 mL, 43.8 mmol) in anhydrous Et_2O (250 mL) were cooled to 0 °C. Ethyl bromoacetate (73.1 g, 48.6 mL, 43.8 mmol) in anhydrous Et_2O (100 mL) was added slowly and the mixture was stirred overnight at 0 °C. Di-*tert*-butyl dicarbonate (43.8 mmol) in anhydrous Et_2O (50 mL) was added and the mixture was stirred at room temperature for 5 hours. 1 M HCl (150 mL) was added to the mixture and the aqueous layer was extracted with Et_2O (4 × 80 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed to give the crude protected α-amino esters. The α-amino ester was treated with 1 M NaOH (438 mL) and LiCl (1.86 g, 43.8 mmol). After stirring at 80 °C for 3 hours and at 20 °C for 1 hour, the solution was extracted with Et_2O (3 × 50 mL). The aqueous layer was acidified with aqueous saturated $KHSO_4$ until the solution reached a pH of 4–5. The aqueous solution was extracted with Et_2O (4 × 100 mL) and the organic layers were dried over $MgSO_4$. After removal of the solvent, the carboxylic acid **12a** was isolated sufficiently pure for further transformations; yield: 7.60 g (66%); ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.25 [2 × s, 9H, C(C*H*$_3$)$_3$], 3.2 (s, 6H, OCH$_3$), 3.08–3.23 [m, 2H, NC*H*$_2$CH(OCH$_3$)$_2$], 3.81 (2 × s, 2H, NC*H*$_2$COOH), 4.15–4.50 [2 × dd, 1H, *J* = 5.37 Hz, 4.88 Hz, C*H*(OCH$_3$)$_2$], 8.80 (br, s, 1H, COO*H*); ^{13}C NMR (68 MHz, $CDCl_3$): δ = 27.7, 27.9 [C(*C*H$_3$)$_3$], 49.1, 49.6 [*C*H$_2$CH(OCH$_3$)$_2$], 49.9, 50.0 (*C*H$_2$COOH), 80.5, 80.6 [*C*(CH$_3$)$_3$], 103.7, 103.9 [*C*H(OCH$_3$)$_2$], 155.2, 155.3 (N*C*O), 173.4, 173.6 (*C*OO); IR (film): 1/λ = 3443 (br, m, OH), 3200 (br, m, OH), 2977 (s), 2939 (s), 2836 (m), 1745 (s, COO), 1702 (s, CON), 1478 (s), 1458 (s), 1395 (s), 1368 (s), 1307 (m), 1252 (m), 1166 (s), 1125 (s), 1077 (s), 1024 (m), 968 (m) cm^{-1}; MS (EI, 80 eV, 80 °C): *m/z* (%) = 263 (2.33, $[M]^+$), 190 (6, $[M - C_4H_9O]^+$), 176 (13, $[M - C_5H_{11}O]^+$), 132 (11, $[M - C_6H_{11}O_3]^+$, 75 (100, $[C_3H_7O_2]^+$); HRMS (80 eV, 40 °C): calcd. for $C_{11}H_{21}NO_6$: 263.13688; found: 263.13885.

N-*tert*-Butyloxycarbonyl-*N*-(2-bromopiperonyl) aminoacetic Acid (12b)

Piperonylamine **11b** (300 mg, 1.31 mmol) and Et_3N (132 mg, 184 μL, 1.31 mmol) in anhydrous THF (20 mL) were cooled to 0 °C. Ethyl bromoacetate (219 mg, 146 μL, 1.31 mmol) in anhydrous THF (5 mL) was added slowly and the mixture was stirred overnight at 0 °C. Di-*tert*-butyl dicarbonate (1.31 mmol) in anhydrous THF (5 mL) was added and the mixture was stirred at room temperature for 5 hours. 1 N HCl (10 mL) was added to the mixture and the aqueous layer was extracted with Et_2O (4 × 20 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under vacuum. The crude material was purified by column chromatography (*n*-hexane/ethyl acetate, 6:1) to give *N*-*tert*-butyloxycarbonyl-*N*-(2-bromopiperonyl) aminoacetic acid ethyl ester as colourless oil; yield: 540 mg (99%); ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.20 (2 × t, 3H, *J* = 7.36 Hz, CH$_2$C*H*$_3$), 1.42 [2 × s, 9H, C(C*H*$_3$)$_3$], 3.83 (2 × s, 2H, NC*H*$_2$Ar), 4.14 (q, 2H, *J* = 7.36 Hz, C*H*$_2$CH$_3$), 4.48 (2 × s, 2H, NC*H*$_2$COO), 5.92 (2 × s, 2H, OC*H*$_2$O), 6.80 (2 × s, 2H, NCH$_2$CC*H*), 6.92 (2 × s, 2H, BrCC*H*); ^{13}C NMR (68 MHz, $CDCl_3$): δ = 14.1, 14.2 (CH$_2$*C*H$_3$), 28.1, 28.2 [C(*C*H$_3$)$_3$], 47.8, 48.5 (N*C*H$_2$Ar), 50.8, 51.3 (N*C*H$_2$COO), 60.9 (*C*H$_2$CH$_3$), 80.6, 80.7 [*C*(CH$_3$)$_3$], 101.7 (O*C*H$_2$O), 108.7, 109.5, 112.4, 112.6, 113.5, 129.7, 147.6 (Ph), 155.5 (N*C*O), 169.6, 169.7 (*C*OOEt); IR ($CHCl_3$): 1/λ = 3019 (s), 2981 (s), 2935 (m), 2901 (m), 1747 (s, COO), 1697 (s, CON), 1504 (s), 1479 (s), 1410 (s), 1455 (s), 1406 (s), 1368 (s), 1216 (s), 1122 (s), 1108 (s), 1040 (s), 956 (m), 935 (s), 896 (m), 862 (m) cm^{-1}; MS (EI, 80 eV, 90 °C): *m/z* (%) = 415 (1.6, $[M]^+$), 336 (4.3, $[M - Br]^+$), 314 (11, $[M - C_5H_9O_2]^+$), 280 (100, $[M - C_4H_8Br]^+$), 234 (14, $[M - C_6H_{14}BrO]^+$), 213 (37, $[C_8H_6BrO_2]^+$); HRMS (80 eV, 30 °C): calcd. for $C_{17}H_{22}NO_6{}^{79}Br$: 415.06304; found: 415.06622.

The ethyl ester (500 mg, 1.20 mmol) was treated with NaOH (0.1 M, 12 mL) and LiCl (63 mg, 1.48 mmol). After stirring at

80 °C for 3 hours and at 20 °C for 1 hour, aqueous saturated $KHSO_4$ was added until the solution displayed a pH of 4–5. The aqueous solution was extracted with Et_2O (4 × 20 mL) and the organic layers were dried over $MgSO_4$. The solvent was evaporated to give protected aminoacetic acid **12b** as colourless crystals; yield: 433 mg (93%); mp 122–123 °C; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.40 [2 × s, 9H, C(CH_3)$_3$], 3.80 (2 × s, 2H, NCH_2COOH), 4.40 (2 × s, 2H, NCH_2Ar), 5.85 (2 × s, 2H, OCH_2O), 6.70 (2 × s, 1H, NCH$_2$CCH), 6.85 (2 × s, 1H, BrCCH), 10.3 (s, 1H, COOH); ^{13}C NMR (68 MHz, $CDCl_3$): δ = 28.0, 28.1 [C(*C*H$_3$)$_3$], 47.5, 48.0 (N*C*H$_2$COOH), 50.7, 51.3 (N*C*H$_2$Ar), 81.0, 81.2 [*C*(CH$_3$)$_3$], 101.7 (O*C*H$_2$O), 108.7, 109.4, 112.4, 112.6, 113.4, 113.8, 129.3, 147.6, 17.7 (Ph), 15.5, 155.8 (*C*ON), 174.2, 174.3 (*C*OOH); IR ($CHCl_3$): 1/λ = 3100 (s, br, COOH), 3018 (s), 2980 (s), 2928 (s), 2896 (s), 2703 (m), 2644 (m), 2567 (m), 1725 (s, COO), 1701 (s, CON), 1504 (s), 1476 (s), 1423 (s), 1398 (s), 1369 (s), 1265 (s), 1216 (s), 1158 (s), 1108 (s), 1040 (s), 959 (m), 934 (s) cm^{-1}; MS (EI, 80 eV, 140 °C): *m/z* (%) = 387 (1.95, [M]$^+$), 331 (1.86, [M – C$_4$H$_8$]$^+$), 314 (2, [M – C$_4$H$_9$O]$^+$), 308 (3.8, [M – Br]$^+$), 286 (9, [M – C$_5$H$_9$O$_2$]$^+$), 252 (100, [M – C$_4$H$_8$Br]$^+$), 213 (40, [C$_8$H$_6$BrO$_2$]$^+$), 57 (90, [C$_4$H$_9$]$^+$); HRMS (80 eV, 120 °C): calcd. for C$_{15}$H$_{18}$NO$_6$^{79}Br: 387.03174; found: 387.03421.

Standard Procedure to Generate Carboxylic Acid Fluorides (for details see Refs.[3,13])

The amino acid (500 mg) in anhydrous CH_2Cl_2 (70 mL) at 0 °C was treated with pyridine (0.6 equivs.) and cyanuric fluoride (0.6 equivs.) with stirring. The mixture was stirred at 0 °C for about 1.5 h (TLC monitoring: 0.5 mL sample of the reaction mixture was quenched with MeOH and detected on a TLC plate with *n*-hexane/ethyl acetate = 1:1).

Work-up method A: Dry pentane (17 mL) was added to complete the precipitation of polar compounds. The solids were filtered off to leave a clear solution. The solvents were carefully removed to give the carboxylic acid fluoride, which was found to be pure enough for further transformations.

Work-up method B: The mixture was quenched with ice/water (50 mL), the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), the combined organic layers were dried over $MgSO_4$, and concentrated to give the amino acid fluoride, which was immediately used without any further purification.

N-tert-Butyloxycarbonyl-*N*-(2,2-dimethoxyethyl)aminoacetyl Fluoride (13a)

Reaction with acid **12a** (500 mg, 1.9 mmol) following the standard procedure, work-up method B to afford **13a** as a pale yellow oil; yield: 480 mg (94.5%); ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.35 [2 × s, 9H, C(CH_3)$_3$], 3.25 (2 × s, 6H, OCH_3), 3.22–3.30 [m, 2H, NCH_2CH(OCH$_3$)$_2$], 4.03 (2 × d, 2H, ^3J[^{1}H,^{19}F] = 3.42 Hz, CH_2COF), 4.20–4.28 [2 × dd, 1H, *J* = 5.37 Hz, 4.88 Hz, CH(OCH$_3$)$_2$]; ^{13}C NMR (68 MHz, $CDCl_3$): δ = 27.7, 27.9 [C(*C*H$_3$)$_3$], 47.7 (2 × d, ^2J[^{13}C,^{19}F] = 68 Hz, *C*H$_2$COF), 50.0, 50.3 [*C*H$_2$CH(OCH$_3$)$_2$], 54.5, 54.6 (O*C*H$_3$), 80.8, 81.1 [*C*(CH$_3$)$_3$], 103.9, 104.0 [*C*H(OCH$_3$)$_2$], 154.3, 154.7 (*C*ON), 157.4 (2 × d, ^1J[^{13}C,^{19}F] = 374 Hz, *C*OF).

N-tert-Butyloxycarbonyl-*N*-(2-bromopiperonyl)aminoacetyl Fluoride (13b)

Reaction with acid **12b** (1.80 g, 4.65 mmol) following the standard procedure, work-up method B to afford **13b** as a pale yellow oil; yield: 1.80 g (99.5%); ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.40 [2 × s, 9H, C(CH_3)$_3$], 3.95–4.12 (2 × d, 2H, ^3J[^{1}H,^{19}F] = 2.94 Hz, CH_2COF), 4.50 (2 × s, 2H, NCH_2Ar), 5.92 (s, 2H, OCH_2O), 6.70–6.85 (2 × s, 1H, NCH$_2$CCH), 6.95 (2 × s, 1H, BrCCH); ^{13}C NMR (68 MHz, $CDCl_3$): δ = 28.0, 28.1 [C(*C*H$_3$)$_3$], 45.4 (2 × d, ^2J[^{13}C,^{19}F] = 68 Hz, *C*H$_2$COF), 50.3, 50.9 (N*C*H$_2$Ar), 81.7 [*C*(CH$_3$)$_3$], 101.8 (O*C*H$_2$O), 109.0, 109,7, 112.5, 112.7, 114.1, 128.8, 147.8, 148.0 (Ph), 154.5 (*C*ON), 157.4 (d, ^1J[^{13}C,^{19}F] = 367 Hz, *C*OF).

Zwitterionic Aza-Claisen Rearrangement (Standard Procedure)

Under argon *N*-allylpyrrolidine and Na_2CO_3 (3 equivs.) in anhydrous CH_2Cl_2 were treated with freshly prepared acid fluoride in anhydrous CH_2Cl_2. Then $AlMe_3$ (2 M in heptane) was injected slowly. A gas was evolved and the mixture darkened to light brown. The mixture was stirred until no reactant remained according TLC control. Then, MeOH was added dropwise and stirring was continued for a further 30 min at 20 °C. The polar side products and salts were filtered off by passing the mixture through a short silica gel column. The filtrate was concentrated and crude material was purified by column chromatography and HPLC (if necessary).

(*R*)-2-Chloropent-4-enoic acid [(2*S*)-methoxycarbonylpyrrolidinyl]amide (14a)

Reaction of allylamine **1a** (500 mg, 2.95 mmol), chloroacetyl chloride **13c** (470 μL, 5.91 mmol, *d* = 1.418, M_R = 113) and $AlMe_3$ (3 mL) following the standard procedure. Reaction temperature −20 °C, reaction time 1 hour. Purification *via* column chromatography (*n*-hexane/ethyl acetate = 3:1) to afford **14a** as a brown oil; yield: 510 mg (70%); $[\alpha]_D^{20}$: −93.7° (*c* 1.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.78–2.25 (m, 4H, NCH$_2$CH_2CH_2), 2.51–2.62 (m, 1H, CHHCH=CH$_2$), 2.72–2.81 (m, 1H, CHHCH=CH$_2$), 3.46–3.60 (m, 1H, NCHH), 3.65 (2 × s, 3H, OCH_3), 3.78–3.85 (m, 1H, NCHH), 4.01, 4.24 (2 × d, 1H, *J* = 7.28 Hz, 5.91 Hz, ClCH), 4.45, 4.62 (2 × d, 1H, *J* = 9.94 Hz, 3.99 Hz, NCHCO$_2$CH$_3$), 5.02–5.14 (m, 2H, CH=CH_2), 5.66–5.79 (2 × dddd, 1H, *J* = 17.18 Hz, 10.17 Hz, 7.14 Hz, 6.88 Hz, CH=CH$_2$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.2, 24.5 (NCH$_2$CH_2), 28.8, 30.8 (NCH$_2$CH$_2$CH_2), 38.0 (*C*H$_2$CH=CH$_2$), 40.7, 54.2 (Cl*C*H), 46.7, 46.8 (N*C*H$_2$), 52.1, 52.7 (CO$_2$CH_3), 58.9, 59.0 (N*C*HCO$_2$), 118.4, 118.7 (CH=*C*H$_2$),), 132.8, 132.9 (*C*H=CH$_2$), 166.7, 167.1 (*C*ON), 171.8, 172.0 (*C*O$_2$CH$_3$); IR (film): 1/λ = 3079 (w), 2980 (m), 2954 (m), 2883 (w),1746 (s, COO), 1660 (s, CON), 1436 (s), 1364 (m), 1337 (m), 1282 (m), 1197 (s), 1175 (s), 1118 (w), 1095 (w), 1044 (w), 998 (m), 924 (m) cm^{-1}; MS (EI, 80 eV, 40 °C): *m/z* (%) = 245 (10, [M]$^+$), 210 (11, [M – Cl]$^+$), 186 (75, [M – C$_2$H$_3$O$_2$]$^+$), 150 (6, [M – C$_2$H$_4$O$_2$Cl]$^+$), 128 (16, [C$_6$H$_{10}$NO$_2$]$^+$), 89 (12, [C$_4$H$_6$Cl]$^+$), 70 (100, [C$_4$H$_8$N]$^+$), 41 (12, [C$_3$H$_5$]$^+$). HRMS: (80 eV, 40 °C): calcd. for C$_{11}$H$_{16}$O$_3$N^{35}Cl: 245.08188; found: 245.08255.

(*R*)-2-Azido-4-(*tert*-butyldimethylsilyloxymethyl)pent-4-enoic Acid [(2*S*)-Methoxycarbonylpyrrolidinyl]amide (14b)

Reaction of *N*-allylproline methyl ester **1b** (1 g, 3.19 mmol) and azidoacetyl fluoride **13d** (1 g, 9.9 mmol, prepared from azidoacetic acid following the standard fluorination procedure, work-up method A)[3] following the standard procedure. Reaction temperature 0 °C, reaction time 3 h. Purification *via* column chromatography (*n*-hexane/ethyl acetate, 3:1) to afford **14b** as a yellow oil; yield: 1.0 g (79%); $[\alpha]_D^{20}$: −75.5° (*c* 2.1, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.01 [s, 6H, Si(CH_3)$_2$], 0.85 [s, 9H, C(CH_3)$_3$], 1.65–2.24 (m, 4H, CH_2CH_2), 2.46–2.68 (m, 2H, N_3CHCH_2), 3.45–3.78 (m, 5H, OCH_3, NCH_2CH$_2$), 3.85–3.94 (m, 1H, NC*H*COO), 4.03–4.22 (m, 2H, TBSOCH_2), 4.40–4.57 (m, 1H, N_3C*H*), 4.99 (2 × s, 1H, C=CH*H*), 5.15 (2 × s, 1H, C=C*H*H); ^{13}C NMR (68 MHz, $CDCl_3$): δ = −5.4 [Si(*C*H$_3$)$_2$], 18.2 [Si*C*(CH$_3$)$_3$], 23.1, 24.6 (*C*H$_2$CH$_2$), 25.8 [SiC(*C*H$_3$)$_3$], 28.9, 29.3 (CH$_2$*C*H$_2$), 33.7 (N_3CH*C*H$_2$), 46.8 (N*C*H$_2$CH$_2$), 52.1, 51.2 (O*C*H$_3$), 57.9, 58.3 (N*C*HCOO), 58.7, 58.9 (N_3*C*H), 65.3, 66.0 (TBSO*C*H$_2$), 112.2, 113.2 (C=*C*H$_2$), 143.2 (*C*=CH$_2$), 168.7, 172.0 (*C*OOCH$_3$); IR ($CHCl_3$): 1/λ = 3079 (w), 2955 (s), 2930 (s), 2885 (m), 2857 (s), 2106 (s, N_3), 1747 (s, COO), 1658 (s, CON), 1472 (m), 1435 (s), 1389 (m), 1362 (m), 1343 (m), 1252 (s), 1197 (s), 1176 (s), 1112 (m), 1006 (m), 939 (w), 908 (m) cm^{-1}; MS (EI, 80 eV, 80 °C): *m/z* (%) = 396 (0.67, $[M]^+$), 381 (0.91, $[M - CH_3]^+$), 354 (5.9, $[M - N_3]^+$), 339 (44, $[M - CH_3N_3]^+$), 223 (100, $[M - C_6H_{15}N_3OSi]^+$), 128 (58, $[C_6H_{10}NO_2]^+$); HRMS (80 eV, 80 °C): calcd. for $C_{18}H_{32}N_4O_4Si$: 396.21928; found: 396.21969.

(*R*)-2-Azidopent-4-enoic Acid [(2*S*)-Methoxycarbonyl-(4*R*)-*tert*-butyldimethylsilyloxypyrrolidinyl]amide (14c)

Reaction of allylamine **1d** (500 mg, 1.67 mmol) and azidoacetyl fluoride **13d** (506 mg, 5.01 mmol, prepared from azidoacetic acid following the standard fluorination procedure, work-up method A)[3] following the general procedure. Reaction temperature 0 °C, reaction time 3 hours. Purification *via* column chromatography (*n*-hexane/ethyl acetate, 3:1) to afford **14c** as colourless crystals; yield: 480 mg (75%); mp 67 °C; $[\alpha]_D^{20}$: −115.4° (*c* 0.5, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.00 [s, 6H, Si(CH_3)$_2$], 0.85 [s, 9H, SiC(CH_3)$_3$], 1.95–2.06 (ddd, 1H, *J* = 13.19 Hz, 12.69 Hz, 2.99 Hz, CH*H*CHCO$_2$CH$_3$), 2.12–2.21 (m, 1H, C*H*HCH-CO$_2$CH$_3$), 2.47–2.67 (ddd, 2H, *J* = 14.65 Hz, 14.16 Hz, 3.17 Hz, CH_2CH=CH$_2$), 3.32–3.42 8 (dd, 1H, *J* = 10.25 Hz, 1.46 Hz, NCH*H*), 3.60–3.80 (m, 5H, OCH_3, NC*H*H, N_3C*H*), 4.45–4.55 (m, 1H, TBSOC*H*), 4.50–4.57 (dd, 1H, *J* = 11.72 Hz, 7.82 Hz, NC*H*CO$_2$CH$_3$), 5.07–5.17 (dd, 1H, *J* = 10.25 Hz, 1.47 Hz, CH=CH*H*), 5.17–5.22 (dd, 1H, *J* = 17.09 Hz, 1.47 Hz, CH=C*H*H), 5.70–5.87 (dddd, 1H, *J* = 17.09 Hz, 10.25 Hz, 7.32 Hz, 6.84 Hz, C*H*=CH$_2$); ^{13}C NMR (68 MHz, $CDCl_3$): δ = −5.0, −4.8 [Si(*C*H$_3$)$_2$], 18.2 [Si*C*(CH$_3$)$_3$], 25.5 [SiC(*C*H$_3$)$_3$], 34.8 (*C*H$_2$CH=CH$_2$), 37.8, 40.0 (*C*H$_2$CHCO$_2$CH$_3$), 52.3 (O*C*H$_3$), 55.2 (N*C*H$_2$), 58.8 (N_3*C*H), 59.6 (N*C*HCO$_2$CH$_3$), 70.5 (TBSO*C*H), 118.9 (CH=*C*H$_2$), 132.3, 132.4 (*C*H=CH$_2$), 168.1 (*C*ON), 172.1 (*C*OOCH$_3$); IR ($CHCl_3$): 1/λ = 3087 (w), 2992 (w), 2953 (m), 2928 (m), 2893 (w), 2856 (m), 2122 (s, N_3), 1765 (s, COO), 1647 (s, CON), 1470 (m), 1462 (m), 1434 (s), 1367 (m), 1324 (w), 1258 (m), 1240 (m), 1202 (m), 1192 (m), 1169 (s), 1150 (m), 1085 (s), 1023 (s), 1004 (m), 974 (m), 924 (m), 915 (m) cm^{-1}; MS (EI, 80 eV, 90 °C): *m/z* (%) = 382 (0.55, $[M]^+$), 367 (1.63, $[M - CH_3]^+$), 325 (100, $[M - C_4H_9]^+$), 258 (12, $[C_{12}H_{24}NO_3Si]^+$); HRMS (80 eV, 90 °C): calcd. for $C_{17}H_{30}N_4O_4Si$: 382.203634; found: 382.20578; calcd. for $C_{16}H_{27}N_4O_4Si$ ($[M - CH_3]^+$): 367.180159; found: 367.18466; calcd. for $C_{13}H_{21}N_4O_4Si$ ($[M - C_4H_9]^+$): 325.133209; found: 325.13534.

(3*S*,6*R*)-6-Allyl-3,4-(2-*tert*-butyldimethylsilyloxyl)propylidene-1,4-piperazine-2,5-dione (15)

Azidopentenoic acid amide **14c** (110 mg, 0.28 mmol) in THF (20 mL) was treated with PPh_3 (91 mg, 0.34 mmol) and H_2O (1 mL). The mixture was stirred at 20 °C for 16 hours. H_2O (10 mL) was added and the aqueous layer was extracted with Et_2O (4 × 15 mL). The combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude material was purified by column chromatography (ethyl acetate) to give piperazine **15** as colourless crystals; yield: 80 mg (85%); mp 139–140 °C; $[\alpha]_D^{20}$: −48.1° (*c* 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.00 [s, 6H, Si(CH_3)$_2$], 0.80 [s, 9H, SiC(CH_3)$_3$], 1.87–1.95 (ddd, 1H, *J* = 12.51 Hz, 12.09 Hz, 4.12 Hz, CH*H*CHOTBS), 2.23–2.30 (dd, 1H, *J* = 12.93 Hz, 5.91 Hz, C*H*HCHOTBS), 2.47–2.61 (m, 2H, CH_2CH=CH$_2$), 3.37 (d, 1H, *J* = 12.92 Hz, NCH*H*CHOTBS), 3.73–3.75 (dd, 1H, *J* = 12.93 Hz, 4.54 Hz, NC*H*HCHOTBS), 3.93–3.99 (m, 1H, NHC*H*), 4.36–4.45 (m, 2H, NHCOC*H*, C*H*OTBS), 5.14–5.23 (m, 2H, CH=CH_2), 5.72–5.83 (dddd, 1H, *J* = 17.32 Hz, 10.17 Hz, 7.44 Hz, 7.15 Hz, C*H*=CH$_2$), 7.30 (br, s, 1H, N*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.0, −4.8 [Si(*C*H$_3$)$_2$], 17.8 [Si*C*(CH$_3$)$_3$], 25.6 [SiC(*C*H$_3$)$_3$], 38.7 (*C*H$_2$CHOTBS), 38.9 (*C*H$_2$CH=CH$_2$), 55.2 (N*C*H$_2$), 56.5 (*C*HOTBS), 57.4 (NH*C*H), 68.2 (NHCO*C*H), 120.2 (CH=*C*H$_2$), 131.7 (*C*H=CH$_2$), 165.2 (N*C*O), 169.8 (NH*C*O); IR (film): 1/λ = 3213 (m), 3165 (w), 3122 (w, NH), 2956 (m), 2928 (m), 2889 (w), 2856 (m), 1680 (s, CONH), 1646 (s, CON), 1498 (w), 1471 (m), 1461 (m), 1439 (m), 1419 (m), 1376 (m), 1361 (w), 1328 (w), 1308 (m), 1285 (w), 1256 (m), 1210 (w), 1161 (w), 1142 (w), 1109 (m), 1086 (m), 1026 (m), 1006 (m), 940 (w), 917 (m) cm^{-1}; MS (EI, 80 eV, 160 °C): *m/z* (%) = 324 (0.17, $[M]^+$), 309 (5, $[M - CH_3]^+$), 267 (100, $[M - C_4H_9]^+$), 239 (67, $[M - C_6H_{13}]^+$); HRMS (80 eV, 160 °C): calcd. for $C_{12}H_{19}N_2O_3Si$ ($[M - C_4H_9]^+$): 267.11649; found: 267.11733.

(*S*)-2-Azidopent-4-enoic Acid [(2*S*)-methoxycarbonylpyrrolidinyl]amide (16)

The chloroamide **14a** (500 mg, 2.04 mmol) in DMF (50 mL) was treated with NaN_3 (600 mg, 9.23 mmol). The mixture was stirred at room temperature for 16 hours. H_2O (20 mL) was added and the aqueous layer was extracted with Et_2O (4 × 10 mL), and the combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude product was purified by column chromatography (*n*-hexane / ethyl acetate, 1:1) to give **16** as a yellow oil; yield: 500 mg (97%); $[\alpha]_D^{20}$: −26.8° (*c* 1.4, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.78–2.01 (m, 3H, NCH$_2$C*H*HCH_2), 2.01–2.20 (m, 1H, NCH$_2$

CH*H*), 2.45–2.66 (m, 2H, CH_2CH=CH_2), 3.31–3.55 (m, 2H, N_3 C*H*, NC*H*H), 3.60 (s, 3H, CO_2CH_3), 3.60–3.69 (m, 1H, NCH*H*), 4.41–4.48 (m, 1H, NCHCO_2CH_3), 5.02–5.11 (d, 1H, J = 10.74 Hz, CH=C*H*H), 5.10–5.21 (d, 1H, J = 17.09 Hz, CH=CH*H*), 5.58–5.86 (2 × dddd, 1H, J = 17.09 Hz, 10.25 Hz, 7.32 Hz, 6.84 Hz, C*H*=CH_2); ^{13}C NMR (68 MHz, $CDCl_3$): δ = 21.9, 24.6 (NCH_2CH_2), 28.7, 31.0 (NCH_2CH_2CH_2), 34.9, 35.5 (*C*H_2CH=CH_2), 46.6, 46.7 (N*C*H_2), 52.0, 52.7 (CO_2CH_3), 58.7, 58.8 (N*C*HCO_2CH_3), 59.1, 59.3 (N_3*C*H), 118.8, 118.9 (CH=*C*H_2), 132.2 (*C*H=CH_2), 168.3 (*C*ON), 171.9 (CO_2CH_3); IR (film): 1/λ = 3078 (w), 2979 (m), 2881 (m), 2841 (w), 2101 (s, N_3), 1746 (s, COO), 1657 (s, CON), 1435 (s), 1363 (m), 1340 (m), 1324 (m), 1280 (m), 1197 (s), 1175 (s), 1119 (w), 1095 (m), 1044 (w), 999 (m) cm^{-1}; MS (EI, 80 eV, 60 °C): *m/z* (%) = 252 (1, $[M]^+$), 224 (1, $[M - N_2]^+$), 221 (1, $[M - CH_3O]^+$), 210 (3, $[M - N_3]^+$), 193 (6, $[M - C_2H_3O_2]^+$), 165 (8, $[M - C_2H_3O_2N_2]^+$), 137 (20, $[M - C_3H_5O_2N_3]^+$),128 (100, $[C_6H_{10}NO_2]^+$), 68 (37, $[C_4H_6N]^+$), 41 (36, $[C_3H_5]^+$); HRMS: (80 eV, 60 °C): calcd. for $C_{11}H_{16}N_4O_3$: 252.12224; found: 252.12422.

(3*S*,6*S*)-6-Allyl-3,4-propylidene-1,4-piperazine-2,5-dione (17)

Azidopentenoic acid amide **16** (200 mg, 0.79 mmol) in THF (20 mL) was treated with PPh_3 (230 mg, 0.87 mmol) and H_2O (1 mL). The mixture was stirred at 20 °C for 16 hours. H_2O (20 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (4 × 15 mL). The combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude material was purified by column chromatography (*n*-hexane/ethyl acetate,1:2) to give piperazinedione **17** as a pale yellow oil; yield. 140 mg (91%); $[\alpha]_D^{20}$: −108.8° (*c* 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.77–1.90 (m, 1H, NCH$_2$C*H*H), 1.90–2.07 (m, 2H, NCH$_2$CH*H*, NCH$_2$CH$_2$C*H*H), 2.22–2.32 (m, 1H, NCH$_2$CH$_2$CH*H*), 2.35–2.44 (m, 1H, C*H*HCH=CH$_2$), 2.77–2.85 (m, 1H, CH*H*CH=CH$_2$), 3.43–3.58 (m, 2H, NCH_2), 3.97–4.02 (dd, 1H, J = 8.39 Hz, 3.30 Hz, C*H*CH$_2$CH=CH$_2$), 4.02–4.09 (dd, 1H, J = 8.94 Hz, 7.56 Hz, NC*H*CO), 5.08–5.17 (m, 2H, CH=CH_2), 5.66–5.76 (m, 1H, C*H*=CH$_2$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.3, (NCH$_2$CH$_2$), 27.9 (NCH$_2$CH$_2$*C*H$_2$), 34.4 (*C*H$_2$CH=CH$_2$), 45.1 (NCH_2), 53.9 (*C*HCH$_2$CH=CH$_2$), 58.8 (N*C*HCO), 119.5 (CH=*C*H$_2$), 132.8 (*C*H=CH$_2$), 164.9 (N*C*O), 169.7 (NH*C*O); IR (film): 1/λ = 3480 (br, m, NH), 3234 (br, m, NH), 3079 (m), 2982 (m), 2954 (m), 2882 (m), 1668 (s, CONH, CON), 1558 (w), 1540 (w), 1429 (s), 1339 (m), 1305 (m), 1276 (m), 1212 (w), 1231 (w), 1212 (w), 1162 (w), 1146 (w), 1119 (w), 1002 (m), 922 (m) cm^{-1}; MS (pos. FAB): *m/z* (%) = 195 (100, $[M+H]^+$), 194 (18, $[M]^+$), 193 (22, $[M - H]^+$), 153 (13, $[M - C_3H_5]^+$), 125 (25, $[M - C_4H_7N]^+$), 69 (96, $[C_4H_7N]^+$), 42 (29, $[C_3H_6]^+$); MS (EI, 80 eV, 40 °C): *m/z* (%) = 194 (56, $[M]^+$), 153 (18, $[M - C_3H_5]^+$), 125 (50, $[C_6H_7NO_2]^+$), 70(100, $[C_4H_8N]^+$), 41 (38, $[C_3H_5]^+$); HRMS (80 eV, 40 °C): calcd. for $C_{10}H_{14}N_2O_2$: 194.10553; found: 194.10633.

(2*R*)-2-[(*N*-*tert*-Butyloxycarbonyl)-*N*-(2,2-dimethoxyethyl)]aminopent-4-enoic Acid [(2*S*)-*tert*-Butyldimethylsilyloxymethylpyrrolidinyl]amide (18a)

Reaction of *N*-allylamine **1a** (500 mg, 1.96 mmol) and acid fluoride **13a** (1.0 g, 3.77 mmol) following the standard procedure. Reaction temperature 0 °C, reaction time 16 hours. After quenching with methanol, the mixture was filtered. The solvent was removed under vacuum. If necessary, reintroduction of the BOC protecting group as follows. The residue was dissolved in THF (30 mL). Di-*tert*-butyl dicarbonate (2 mmol) was added and the mixture was stirred at room temperature for 16 hours. H_2O (20 mL) was added and the aqueous layer was extracted with Et_2O (4 × 20 mL). The combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude material was purified by column chromatography (*n*-hexane/ethyl acetate, 1:1) to give **18a** as a yellow oil; yield: 710 mg (72%); $[\alpha]_D^{20}$: +14.9° (*c* 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.00 [s, 6H, Si(CH_3)$_2$], 0.80 [s, 9H, SiC(CH_3)$_3$], 1.40 [s, 9H, NCOOC(CH_3)$_3$], 1.71–2.05 (m, 4H, NCH$_2$CH_2CH_2), 2.36–2.49 (m, 1H, C*H*HCH=CH$_2$), 2.49–2.57 (m, 1H, CH*H*CH=CH$_2$), 3.08–3.81 [m, 12H, CH_2OSi, CH(OCH_3)$_2$, NCH_2CH$_2$, NCH_2CH(OCH$_3$)$_2$], 4.02–4.18 (m, 1H, NC*H*CH$_2$OSi), 4.38–4.58 [m, 1H, C*H*(OCH$_3$)$_2$], 4.60–4.67 and 4.83–4.91 (2 × m, 1H, C*H*CH$_2$CH=CH$_2$), 4.94–5.02 (d, 1H, J = 10.04 Hz, CH=C*H*H), 5.03–5.10 (d, 1H, J = 17.18 Hz, CH=CH*H*), 5.62–5.77 (m, 1H, C*H*=CH$_2$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.5 [Si(*C*H$_3$)$_2$], 18.0 [Si*C*(CH$_3$)$_3$], 24.1 (NCH*C*H$_2$CH$_2$), 25.8 [SiC(*C*H$_3$)$_3$], 26.5 (NCHCH$_2$*C*H$_2$), 28.2 [NCOOC(*C*H$_3$)$_3$), 34.4 (*C*H$_2$CH=CH$_2$), 44.6, 45.6 [N*C*H$_2$CH(OCH$_3$)$_2$], 46.8 (*C*H$_2$OSi), 53.3, 53.7 [CH(O*C*H$_3$)$_2$], 53.9 (*C*HCH$_2$CH=CH$_2$), 58.7 (N*C*HCH$_2$OSi), 62.3, 65.0 (*C*H$_2$OSi), 80.2 [NCOO*C*(CH$_3$)$_3$], 103.1 [*C*H(OCH$_3$)$_2$], 117.0 (CH=*C*H$_2$), 134.4, 134.7 (*C*H=CH$_2$), 154.9, 155.7 [N*C*OOC(CH$_3$)$_3$], 176.5 (*C*ON); IR (film): 1/λ = 3076 (w), 2954 (s), 2930 (s), 2884 (m), 2758 (m), 1695 (s, OCON), 1648 (s, CON), 1471 (m), 1438 (m), 1402 (m), 1390 (m), 1366 (m), 1348 (w), 1308 (w), 1253 (m), 1168 (m), 1125 (s), 1079 (m), 1025 (w), 996 (w), 977 (w) cm^{-1}; MS (EI, 80 eV, 90 °C): *m/z* (%) = 500 (3, $[M]^+$), 485 (10, $[M - CH_3]^+$), 468 (5, $[M - CH_4O]^+$), 443 (16, $[M - C_4H_9]^+$), 429 (8, $[M - C_5H_{11}]^+$), 413 (13, $[M - C_5H_{11}O]^+$), 369 (23, $[M - C_6H_{11}O_3]^+$), 355 (78, $[M - C_7H_{17}OSi]^+$), 299 (17, $[M - C_{11}H_{25}OSi]^+$); HRMS: (80 eV, 90 °C): calcd. for $C_{25}H_{48}N_2O_6Si$: 500.32816; found: 500.32655.

(2*R*)-2-[*N*-(2-Bromo-4,5-methylenedioxyphenyl)methyl]-*N*-(*tert*-butyloxycarbonyl)-aminopent-4-enoic Acid [(2*S*)-*tert*-butyldimethylsilyloxymethyl-pyrrolidinyl]amide (18b)

Reaction of *N*-allylamine **2b** (1.0 g, 4.33 mmol) and acid fluoride **13b** (2.5 g, 8.66 mmol) following the standard procedure. Reaction temperature 0 °C, reaction time 20 hours. If necessary reintroduction of the BOC protecting group. The crude material was dissolved in CH_2Cl_2 (30 mL). Et_3N (1.2 mL) and di-*tert*-butyl dicarbonate (4.5 mmol) were added. The mixture was stirred for 3 hours. H_2O (20 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), and the combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude material was purified by column chromatography (*n*-hexane/ethyl acetate, 6:1) to give **18b** as a pale yel-

low oil; yield: 1.79 g (82%); $[\alpha]_D^{20}$: +12.5° (*c* 1.6, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.00 [s, 6H, Si(C*H*$_3$)$_2$], 0.85 [s, 9H, SiC(C*H*$_3$)$_3$], 1.40, 1.50 [2 × s, 9H, OC(C*H*$_3$)$_3$], 1.55–2.02 (m, 4H, C*H*$_2$C*H*$_2$), 2.30–2.45 (ddd, 1H, *J* = 14.71 Hz, 7.36 Hz, 7.35 Hz, CH*H*CH=CH$_2$), 2.46–2.66 (dd, 1H, *J* = 13.97 Hz, 7.35 Hz, C*H*HCH=CH$_2$), 2.88, 3.13 (2 × m, 1H, NCH*H*CH$_2$), 3.40–3.69 (m, 3H, NC*H*HCH$_2$, OC*H*$_2$), 4.05 (m, 1H, NC*H*CH$_2$), 4.20–4.56 (m, 2H, ArC*H*$_2$), 4.97–5.25 (m, 3H, BOCNC*H*, CH=C*H*$_2$), 5.61–5.81 (m, 1H, C*H*=CH$_2$), 5.90 (2 × s, 2H, OC*H*$_2$O), 6.35, 6.55 (2 × s, 1H, NCH$_2$CC*H*), 6.90 (2 × s, 1H, BrCC*H*); ^{13}C NMR (68 MHz, $CDCl_3$): δ = −5.5 [Si(*C*H$_3$)$_2$], 18.0, 18.2 [Si*C*(CH$_3$)$_3$], 23.8 (*C*H$_2$CH$_2$), 25.8, 25.9 [SiC(*C*H$_3$)$_3$], 26.5, 27.3 (CH$_2$*C*H$_2$), 28.0, 28.2 [OC(*C*H$_3$)$_3$], 34.2 (*C*H$_2$CH=CH$_2$), 46.8, 47.1 (N*C*H$_2$CH$_2$), 55.6 (N*C*H), 58.1 (NCHCH$_2$OTBS), 58.6 (TBSO*C*H$_2$), 61.6 (N*C*H$_2$Ar), 80.5 (O*C*(CH$_3$)$_3$), 101.4 (O*C*H$_2$O), 107.0, 118.0, 133.8, 146.6 (Ar), 112.4 (CH=*C*H$_2$), 133.9 (*C*H=CH$_2$), 155.6 (O*C*ON), 168.6 (*C*ON); IR (film): 1/λ = 3077 (w), 2954 (s), 2929 (s), 2883 (s), 2857 (s), 1694 (s, OCON), 1649 (s, CON), 1503 (s), 1480 (s), 1449 (s), 1412 (s), 1400 (s), 1391 (s), 1367 (s), 1342 (m), 1310 (s), 1252 (s), 1163 (s), 1102 (s), 1038 (s), 996 (m), 963 (m) cm^{-1}; MS (EI, 80 eV, 160 °C): *m/z* (%) = 624 (8.8, $[M]^+$), 568 (8.2, $[M - C_4H_8]^+$), 523 (7.4, $[M - C_5H_9O_2]^+$), 511 (17, $[M - C_6H_{15}Si]^+$), 489 (6.4, $[M - C_4H_8Br]^+$), 445 (8.6, $[M - C_5H_8O_2Br]^+$), 297 (93, $[M - C_{14}H_{20}O_2BrSi]^+$), 213 (90, $[C_8H_6O_2Br]^+$), 70 (100, $[C_4H_8N]^+$), 57 (85, $[C_4H_9]^+$); HRMS: (80 eV, 160 °C): calcd. for $C_{29}H_{45}N_2O_6Si^{79}Br$: 624.22302; found: 624.22631.

(2*S*)-2-[*N*-(2-Bromo-4,5-methylenedioxyphenyl)methyl]-*N*-(tert-butyloxycarbonyl)-aminopent-4-enoic Acid [(2*S*)-*tert*-Butyldimethylsilyloxymethyl-pyrrolidinyl]amide (*epi*-18b)

Amide **18b** (250 mg) was dissolved in DMF (10 mL) and treated with Na_2CO_3 (5 equivs.). The reaction mixture was refluxed for 20 h. After cooling to room temperature, H_2O was added and the aqueous layer was extracted with Et_2O. The combined organic layers were dried over $MgSO_4$. After removal of the solvent, the diastereomers were separated by means of HPLC: (20% ethyl acetate/*n*-hexane, Nucleosil 50–5, 32 × 110 mm, flow 64 mL/min, retention time: $t_{epi\text{-}18b}$ = 6.86 min, t_{18b} = 8.09 min); yield: 90 mg **18b** (36%) and 140 mg *epi*-**18b** (56%). Data of amide *epi*-**18b**: $[\alpha]_D^{20}$: −52.8° (*c* 1.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.00 [s, 6H, Si(C*H*$_3$)$_2$], 0.80 [s, 9H, SiC(C*H*$_3$)$_3$], 1.30 [s, 9H, OC(C*H*$_3$)$_3$], 1.70–2.15 (m, 4H, C*H*$_2$C*H*$_2$), 2.35–2.58 (m, 2H, C*H*$_2$CH=CH$_2$), 3.36–3.62 (m, 2H, NCH*H*CH$_2$, OCH*H*), 3.62–3.81 (m, 2H, NC*H*HCH$_2$, OC*H*H), 3.90 (m, 1H, BOCNC*H*), 4.35 (d, 1H, *J* = 16.92 Hz, NCH*H*Ar), 4.51 (d, 1H, *J* = 16.92 Hz, NC*H*HAr), 4.96–5.15 (m, 3H, NC*H*, CH=C*H*$_2$), 5.60–5.77 (m, 1H, C*H*=CH$_2$), 5.90 (s, 2H, OC*H*$_2$O), 6.50 (s, 1H, Ar-H), 6.90 (s, 1H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.5 [Si(*C*H$_3$)$_2$], 18.0 [Si*C*(CH$_3$)$_3$], 22.1, 24.5 (*C*H$_2$CH$_2$), 25.7 [SiC(*C*H$_3$)$_3$], 26.8, 27.3 (CH$_2$*C*H$_2$), 28.0 [OC(*C*H$_3$)$_3$], 31.5 (N*C*HCH$_2$OTBS), 34.3 (*C*H$_2$CH=CH$_2$), 46.9, 47.4 (N*C*H$_2$CH$_2$), 55.2 (N*C*H), 58.6 (TBSO*C*H$_2$), 62.4 (N*C*H$_2$Ar), 80.5 [O*C*(CH$_3$)$_3$], 101.4 (O*C*H$_2$O), 106.7, 118.1, 132.1, 147.1 (Ar), 112.3 (CH=*C*H$_2$), 133.5 (*C*H=CH$_2$), 155.6 (O*C*ON), 168.6 (*C*ON); IR ($CHCl_3$): 1/λ = 3070 (w), 3017 (s), 2976 (s), 2956 (s), 2930 (s), 2885 (s), 2858 (s), 1812 (w), 1682 (s, OCON), 1642 (s, CON), 1504 (s), 1480 (s), 1452 (s), 1412 (s), 1368 (s), 1340 (m), 1313 (m), 1216 (s), 1161 (s), 1105 (s), 1041 (s), 999 (m) cm^{-1}; MS (EI, 80 eV, 140 °C): *m/z* (%) = 624 (16, $[M]^+$), 567 (11, $[M - C_4H_9]^+$), 523 (13, $[M - C_5H_9O_2]^+$), 511 (30, $[M - C_6H_{15}Si]^+$), 297 (100, $[M - C_{14}H_{20}O_2BrSi]^+$), 213 (97, $[C_8H_6O_2Br]^+$), 70 (25, $[C_4H_8N]^+$), 57 (15, $[C_4H_9]^+$). HRMS (80 eV, 140 °C): calcd. for $C_{29}H_{45}N_2O_6Si^{79}Br$: 624.22302; found: 624.22564.

(*R*)-2-Chloropent-4-enoic Acid [(2*S*)-*tert*-Butyldimethylsilyloxymethylpyrrolidinyl]amide (18c)

Reaction of allylamine **2a** (500 mg, 1.96 mmol), chloroacetyl chloride **13c** (310 μL, 3.89 mmol, *d* = 1.418, M_R = 113) and $AlMe_3$ (2 mL) following the standard procedure. Reaction temperature −20 °C, reaction time 1 hour. Purification *via* column chromatography (*n*-hexane/ethyl acetate, 7:1) to afford **18c** as a pale yellow oil; yield: 450 mg (69%); $[\alpha]_D^{20}$: −72.5° (*c* 3.0, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 0.00 [s, 6H, Si(CH$_3$)$_2$], 0.70 [s, 9H, SiC(CH$_3$)$_3$], 1.68–2.10 (m, 4H, NCH$_2$C*H*$_2$C*H*$_2$), 2.49–2.71 (m, 2H, C*H*$_2$CH=CH$_2$), 3.29–3.50 (m, 2H, NC*H*$_2$), 3.50–3.71 (m, 2H, OC*H*$_2$), 4.01–4.18 (m, 1H, NC*H*), 4.18–4.23, 4.50–4.62 (2 × m, 1H, ClC*H*), 5.01–5.15 (m, 2H, CH=C*H*$_2$), 5.64–5.81 (m, 1H, C*H*=CH$_2$); ^{13}C NMR (68 MHz, $CDCl_3$): δ = −5.5, −5.6 [Si(*C*H$_3$)$_2$], 17.9, 18.2 [Si*C*(CH$_3$)$_3$], 21.7, 24.0 (NCH$_2$*C*H$_2$CH$_2$), 25.6, 25.7 [SiC(*C*H$_3$)$_3$], 26.7, 27.8 (NCH$_2$CH$_2$*C*H$_2$), 38.0, 38.1 (*C*H$_2$CH=CH$_2$), 45.7, 47.1 (N*C*H$_2$), 54.5, 54.6 (N*C*H), 58.5, 58.7 (NCH*C*H$_2$OTBS), 61.8, 65.2 (Cl*C*H), 118.4 (CH=*C*H$_2$), 133.2 (*C*H=CH$_2$), 166.6, 167.3 (*C*ON); IR (film): 1/λ = 3080 (w), 2954 (s), 2929 (s), 2883 (m), 2856 (m), 1652 (s, CON), 1576 (w), 1558 (w), 1539 (w), 1521 (w), 1471 (m), 1436 (s), 1386 (w), 1360 (w), 1340 (w), 1254 (m), 1189 (w), 1165 (w), 1102 (m), 1054 (m), 997 (m), 920 (m), 836 (s, CCl) cm^{-1}; MS (EI, 80 eV, 70 °C): *m/z* (%) = 331 (0.62, $[M]^+$), 316 (3, $[M - CH_3]^+$), 296 (1, $[M - Cl]^+$), 274 (100, $[M - C_4H_9]^+$), 186 (19, $[M - C_7H_{17}OSi]^+$), 70 (53, $[C_4H_8N]^+$); HRMS: (80 eV, 70 °C): calcd. for $C_{16}H_{30}NO_2Si^{35}Cl$: 331.17343; found: 331.17466; calcd. for $C_{15}H_{27}NO_2Si^{35}Cl$ ($[M - CH_3]^+$): 316.14996; found: 316.14866; calcd. for $C_{12}H_{21}NO_2Si^{35}Cl$ ($[M - C_4H_9]^+$): 274.10300; found: 274.10288.

(*R*)-2-Azidopent-4-enoic Acid [(2*S*)-*tert*-Butyldiphenylsilyloxymethylpyrrolidinyl]amide (18d)

Reaction of allylamine **2b** (540 mg, 1.42 mmol) and azidoacetyl fluoride **13d** (510 mg, 4.95 mmol, prepared from azidoacetic acid following the standard fluorination procedure, work-up method A)[3] following the standard procedure. Reaction temperature 0 °C, reaction time 3 hours. Purification *via* column chromatography (*n*-hexane/ethyl acetate, 5:1) to afford **18d** as a yellow oil; yield: 500 mg (76%); $[\alpha]_D^{20}$: −49.1° (*c* 1.9, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.05 [s, 9H, SiC(C*H*$_3$)$_3$], 1.80–2.20 (m, 4H, C*H*$_2$C*H*$_2$), 2.4–2.7 (2 × m, 1H, NCH*H*CH$_2$), 3.35–3.50 (m, 2H, C*H*$_2$CH=CH$_2$), 3.50–3.60 (m, 1H, NC*H*HCH$_2$), 3.70–3.82 (m, 2H, NC*H*, OCH*H*), 3.83–3.95 (m, 1H, OC*H*H), 4.20–4.36 (m, 1H, N$_3$C*H*), 5.12–5.19 (2 × d, 1H, *J* = 11.23 Hz, CH=CH*H*), 5.20–5.29 (2 × d, 1H, *J* = 17.09 Hz, CH=C*H*H), 5.73–5.90 (2 × dddd, 1H, *J* = 17.09 Hz, 11.23 Hz, 7.32 Hz, 6.84 Hz, C*H*=CH$_2$); ^{13}C NMR

(68 MHz, $CDCl_3$): δ = 19.0, 19.1 [Si*C*(CH_3)$_3$], 21.4, 24.1 (*C*H_2CH$_2$), 26.7, 26.9 [SiC(*C*H_3)$_3$], 27.9 (CH_2*C*H_2), 34.6, 34.8 (*C*H_2CH=CH_2), 45.8, 47.2 (NCH_2CH_2), 58.3, 58.5 (NC*H*), 58.6, 59.4 (N_3C*H*), 63.2, 64.8 (*C*H_2O), 118.7 (CH=*C*H_2), 127.5, 129.5, 129.9, 132.0, 132.6, 134.9, 135.4 (Ph), 132.7, 133.3 (*C*H=CH_2), 167.4, 167.7 (*C*ON); IR (film): 1/λ = 3070 (m), 3048 (m), 2958 (s), 2930 (s), 2857 (s), 2245 (w), 2100 (N_3), 1827 (w), 1749 (w), 1651 (CON), 1588 (w), 1567 (w), 1471 (m), 1428 (s), 1390 (m), 1360 (m), 1341 (m), 1260 (m), 1235 (m), 1192 (m), 1164 (w), 1113 (s), 1054 (m), 997 (m) cm^{-1}; MS (EI, 80 eV, 130 °C): *m/z* (%) = 462 (0.58, $[M]^+$), 447 (0.32, $[M - CH_3]^+$), 434 (0.77, $[M - N_2]^+$), 405 (100, $[M - C_4H_9]^+$), 377 (8, $[M - C_4H_9N_2]^+$), 310 (14, $[M - C_{12}H_8]^+$), 280 (11, $[M - C_{14}H_{14}]^+$); HRMS (80 eV, 130 °C): calcd. for $C_{26}H_{34}N_4O_2Si$: 462.24510; found: 462.24298.

(*S*)-2-Azidopent-4-enoic Acid [(2*S*)-*tert*-Butyldimethylsilyloxymethylpyrrolidinyl]amide (19)

Chloroamide **18c** (200 mg, 0.60 mmol) in DMF (20 mL) was treated with NaN_3 (200 mg, 3.07 mmol). The mixture was stirred at room temperature for 16 hours. H_2O (20 mL) was added and the aqueous layer was extracted with Et_2O (4 × 10 mL), and the combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude product was purified by column chromatography (*n*-hexane/ethyl acetate, 5:1) to give **19** as a yellow oil; yield: 200 mg (99%); $[\alpha]_D^{20}$: −4.2° (*c* 2.1, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.00 [s, 6H, Si(C*H*$_3$)$_2$], 0.85 [s, 9H, SiC(C*H*$_3$)$_3$], 1.72–2.11 (m, 4H, C*H*$_2$ C*H*$_2$), 2.05 (m, 2H, CH_2=CHC*H*$_2$), 3.31–3.52 (m, 3H, NC*H*H, CH*H*O, NC*H*CH$_2$O), 3.52–3.78 (m, 2H, NCH*H*, C*H*HO), 3.78–3.85, 4.08–4.10 (2 × m, 1H, N_3C*H*), 5.11 (d, 1H, *J* = 10.26 Hz, CH=CH*H*), 5.18 (dt, 1H, *J* = 17.08 Hz, 1.47 Hz CH=C*H*H), 5.75 (dddd, 1H, *J* = 17.08 Hz, 10.26 Hz, 7.33 Hz, 6.84 Hz, C*H*=CH_2); ^{13}C NMR (68 MHz, $CDCl_3$): δ = −5.6 (Si*C*H$_3$), 17.9 [SiC(*C*H$_3$)$_3$], 21.5, 24.3 (NCH$_2$*C*H$_2$CH$_2$), 25.6, 25.7 [SiC(*C*H$_3$)$_3$], 26.7, 28.1 (NCH$_2$CH$_2$*C*H$_2$), 35.2, 35.6 (*C*H$_2$ CH=CH_2), 45.7, 47.4 (N*C*H$_2$CH$_2$), 58.6, 58.8 (N*C*HCH$_2$O), 59.1 (*C*H$_2$OTBS), 62.3, 64.5 (N_3*C*H), 118.7, 118.8 (CH=*C*H$_2$), 132.5 (*C*H=CH_2), 168.9 (N*C*O); IR (film): 1/λ = 3080 (w), 2954 (s), 2929 (s), 2883 (m), 2857 (s), 2099 (s, N_3), 1652 (s, CON), 1471 (m), 1462 (m), 1429 (s), 1381 (w), 1360 (w), 1319 (w), 1257 (s), 1193 (w), 1165 (w), 1103 (s), 1055 (m), 1004 (m), 956 (w), 919 (m) cm^{-1}; MS (EI, 80 eV, 70 °C): *m/z* (%) = 338 (0.36, $[M]^+$), 323 (1, $[M - CH_3]^+$), 310 (2, $[M - N_2]^+$), 281 (100, $[M - C_4H_9]^+$), 253 (32, $[M - C_4H_6N_3]^+$), 242 (21, $[C_{12}H_{24}NO_2]^+$); HRMS: (80 eV, 70 °C): calcd. for $C_{15}H_{27}N_4O_2Si$ ($[M - CH_3]^+$): 323.19034; found: 323.19111; calcd. for $C_{16}H_{30}N_2O_2Si$ ($[M - N_2]^+$): 310.20764; found: 310.20833; calcd. for $C_{12}H_{21}N_4O_2Si$ ($[M - C_4H_9]^+$): 281.14337; found: 281.14533.

(3*R*)-3-Allyl-(*N*-tert-butyloxycarbonyl)-6,7-methylenedioxy-1,2,3,4-tetrahydro-4-isoquinolone (20)

Under argon, *N*-piperonylprolinol silyl ether amide **18b** (500 mg, 0.80 mmol) in anhydrous THF (20 mL) was cooled to −78 °C. BuLi (575 μL, 0.92 mmol, 1.6 M in hexane) was injected dropwise. The temperature was raised to −40 °C and the mixture was stirred under these conditions for a further 3 hours (TLC monitoring). Saturated aqueous NH_4Cl (10 mL) was added to the mixture, the aqueous layer was extracted with Et_2O (4 × 10 mL), and the combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude material was purified by column chromatography (*n*-hexane/ethyl acetate, 5:1) to give **20** as a yellow oil; yield: 110 mg (41.5%); $[\alpha]_D^{20}$: −4.7° (*c* 1.3, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.40 [s, 9H, C(C*H*$_3$)$_3$], 2.30–2.55 (m, 2H, CH_2=CHC*H*$_2$), 4.12–4.35 (m, 1H, NC*H*CO), 4.65–5.25 (m, 4H, NC*H*$_2$Ar, CH=C*H*$_2$), 5.62–5.87 (m, 1H, C*H*=CH_2), 5.98 (s, 2H, OC*H*$_2$O), 6.60 (s, 1H, Ar-H), 7.35 (s, 1H, Ar-H); ^{13}C NMR (68 MHz, $CDCl_3$): δ = 28.2 [C(*C*H$_3$)$_3$], 34.4 (CH_2=CH*C*H$_2$), 40.8 (N*C*HCO), 60.1 (N*C*H$_2$Ar), 80.7 [*C*(CH$_3$)$_3$], 101.9 (O*C*H$_2$O), 105.3, 106.1, 147.6, 152.7, 154.2 (Ar), 118.3 (CH=*C*H$_2$), 133.5 (*C*H=CH_2), 192.8 (*C*O); IR ($CHCl_3$): 1/λ = 3019 (s), 2978 (m), 2900 (w), 1681 (s, CO), 1619 (m), 1505 (m), 1482 (s), 1412 (s), 1369 (m), 1350 (w), 1316 (m), 1282 (m), 1245 (s), 1215 (s), 1162 (s), 1122 (w), 1041 (m) cm^{-1}; MS (EI, 80 eV, 110 °C): *m/z* (%) = 331 (1.26, $[M]^+$), 290 (17, $[M - C_3H_5]^+$), 274 (1.59, $[M - C_4H_9]^+$), 258 (3, $[M - C_4H_9O]^+$), 234 (12, $[M - C_7H_{13}]^+$), 190 (62, $[M - C_8H_{13}O]^+$), 57 (100, $[C_4H_9]^+$); HRMS (80 eV, 100 °C): calcd. for $C_{18}H_{21}NO_5$: 331.14197; found: 331.14422.

(3*R*,4*R*)-3-Allyl-*N*-(2,2-diethoxyethyl)-4-hydroxy-4-trimethylsilylmethyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline (21) and (3*R*)-3-Allyl-*N*-(2,2-diethoxyethyl)-4-methylene-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline (22)

Under argon, isoquinolone **6** (250 mg, 0.72 mmol)[3a] in anhydrous THF (10 mL) was cooled to −78 °C. Trimethylsilylmethyllithium (870 μL, 0.87 mmol, 1 M in heptane) was injected dropwise. The mixture was stirred at −78 °C for 3 hours (TLC monitoring). Saturated aqueous NH_4Cl (10 mL) was added to the mixture, the aqueous layer was extracted with Et_2O (4 × 10 mL), and the combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude material was purified by column chromatography (*n*-hexane/ethyl acetate, 7:1) to afford carbinol **21** as a yellow oil; yield: 240 mg (76.6%). Data of carbinol **21**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.00 [s, 9H, Si(C*H*$_3$)$_3$], 1.12 [2 × t, 6H, *J* = 7.35 Hz, (C*H*$_3$CH$_2$O)$_2$], 1.35 (d, 1H, *J* = 4.71 Hz, SiCH*H*), 1.63 (d, 1H, *J* = 5.44 Hz, SiC*H*H), 1.84 (s, 1H, O*H*), 2.10–2.19 (m, 1H, CH*H*CH=CH_2), 2.28–2.36 (m, 1H, C*H*HCH=CH_2), 2.68–2.75 (dd, 1H, *J* = 13.24 Hz, 5.15 Hz, NCH*H*CH), 2.78–2.85 (dd, 1H, *J* = 13.24 Hz, 5.15 Hz, NC*H*HCH), 2.99–3.03 (dd, 1H, *J* = 6.61 Hz, 5.89 Hz, NC*H*), 3.46–3.57 (m, 2H, CH$_3$C*H*$_2$O), 3.60–3.70 (m, 3H, CH$_3$C*H*$_2$O, NCH*H*Ar), 3.82 (d, 1H, *J* = 5.44 Hz, NC*H*HAr), 4.57 (t, 1H, *J* = 5.15 Hz, C*H*(OEt)$_2$), 4.93–5.05 (m, 2H, CH=C*H*$_2$), 5.85 (2 × s, 2H, OC*H*$_2$O), 5.90–6.00 (m, 1H, C*H*=CH_2), 6.40 (s, 1H, Ar-H), 7.04 (s, 1H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 0.4, 0.6 [Si(*C*H$_3$)$_3$], 15.3 (*C*H$_3$CH$_2$O), 28.8 (*C*H$_2$CH=CH_2), 34.0 (Si*C*H$_2$), 51.2 (N*C*H$_2$Ar), 57.7 (N*C*H$_2$CH), 61.6, 62.1 (CH$_3$*C*H$_2$O), 67.6 (N*C*H), 76.7 (HO*C*), 100.6 (O*C*H$_2$O), 100.9 (*C*H(OEt)$_2$), 105.1, 106.8, 126.0, 136.5, 146.1, 146.4 (Ar), 115.7 (CH=*C*H$_2$), 138.7 (*C*H=CH_2).

Elimination Method A: Under argon, NaH (14 mg, 0.47 mmol, 80% in mineral oil) in anhydrous THF (10 mL) was cooled to 0 °C. Isoquinoline **21** (170 mg, 0.39 mmol) in anhydrous THF (10 mL) was added. The mixture was stirred at 0 °C for 1 hour and then refluxed for a further 3 hours. The mix-

ture was cooled to 0 °C again, saturated aqueous NH_4Cl (10 mL) was added dropwise. The aqueous layer was extracted with Et_2O (4 × 10 mL), and the combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude material was purified by column chromatography (*n*-hexane/ethyl acetate, 6:1) to give **22** as a yellow oil; yield: 110 mg (81.5%).

Elimination Method B: Isoquinoline **21** (150 mg, 0.34 mmol) in dry $CHCl_3$ (10 mL) was treated with acetic acid (5 mL). The mixture was stirred at 20 °C for 3 hours (TLC monitoring). Saturated aqueous K_2CO_3 was added until the solution reached a pH of 10. The aqueous layer was extracted with $CHCl_3$ (4 × 10 mL), the combined organic layers were dried over Na_2SO_4. The solvent was evaporated, and the crude material was purified by column chromatography (*n*-hexane/ethyl acetate, 6:1) to give **22** as yellow oil; yield: 100 mg (85%); $[\alpha]_D^{20}$: +31.0° (*c* 1.7, $CHCl_3$). Data of olefin **22**: ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.20 [2 × t, 6H, *J* = 7.35 Hz, $(CH_3CH_2O)_2$], 2.06–2.20 (m, 1H, CH*H*CH=CH_2), 2.30–2.42 (m, 1H, C*H*HCH=CH_2), 2.60–2.66 (dd, 2H, *J* = 5.15 Hz, 4.68 Hz, NCH_2CH), 3.36–3.44 (dd, 1H, *J* = 8.09 Hz, 6.62 Hz, NC*H*), 3.44–3.68 (m, 4H, $(CH_3CH_2O)_2$), 3.68–3.78 (d, 1H, *J* = 6.91 Hz, NCH*H*Ar), 3.96–4.07 (d, 1H, *J* = 7.65 Hz, NC*H*HAr), 4.59 (t, 1H, *J* = 5.15 Hz, C*H*$(OEt)_2$), 4.79 (s, 1H, CH*H*=C), 4.91–5.03 (m, 2H, CH=CH_2), 5.35 (s, 1H, C*H*H=C), 5.70–5.90 (m, 1H, C*H*=CH_2), 5.85 (s, 2H, OCH_2O), 6.43 (s, 1H, Ar-H), 7.04 (s, 1H, Ar-H); ^{13}C NMR (68 MHz, $CDCl_3$): δ = 15.3 [$(CH_3CH_2O)_2$], 35.0 (CH_2CH=CH_2), 50.6 (NCH_2CH), 56.7 (NCH_2Ar), 61.9, 62.0 [$(CH_3CH_2O)_2$], 65.1 (NCH), 100.7 (OCH_2O), 102.6 [CH$(OEt)_2$], 103.8, 106.0, 125.6, 127.2, 146.6, 147.6 (Ar), 107.8 (CH_2=C), 115.8 (CH=CH_2), 136.1 (CH=CH_2), 140.1 (CH_2=C); IR ($CHCl_3$): 1/λ = 3019 (s), 2977 (m), 2896 (m), 1504 (m), 1482 (s), 1421 (w), 1389 (w) cm^{-1}; MS (EI, 80 eV, 80–100 °C): *m/z* (%) = 344 (0.1, $[M - H]^+$), 304 (100, $[M - C_3H_5]^+$), 300 (15, $[M - OC_2H_5]^+$), 242 (32, $[M - C_5H_{11}O_2]^+$), 103 (24, $[C_5H_{11}O_2]^+$), 75 (25, $[C_3H_7O_2]^+$); HRMS (80 eV, 100 °C): calcd. for $C_{17}H_{22}NO_4$ ($[M - C_3H_5]^+$): 304.15488; found: 304.15643.

(3*R*,4*R*)-3,4-Diallyl-*N*-(2,2-diethoxyethyl)-4-hydroxy-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline (23)

Under argon, allyltriphenyltin (576 mg, 1.47 mmol) was dissolved in anhydrous THF (3 mL). Phenyllithium (816 μL, 1.47 mmol, 1.8 M in cyclohexane/ether) was added. The mixture was stirred at 20 °C for 30 minutes, during this time a white precipitate occurred and the mixture changed from colourless to green. The so formed allyllithium was then cooled to −78 °C and isoquinolone **6** (390 mg, 1.27 mmol) was injected dropwise. The mixture was stirred at −60 °C for a further 1 hour (TLC monitoring). Methanol (10 mL) was added and the solid was filtered off. The solvent was evaporated, and the crude material was purified by column chromatography (*n*-hexane/ethyl acetate, 6:1) to give diallylisoquinoline **23** as a yellow oil; yield: 390 mg (88%); $[\alpha]_D^{20}$: +87.2° (*c* 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.12 [2 × t, 6H, *J* = 6.59 Hz, $(CH_3CH_2O)_2$], 2.05 (s, 1H, O*H*), 2.09–2.16 (m, 1H, NCHCH*H*), 2.16–2.25 (m, 1H, NCHC*H*H), 2.40–2.46 (dd, 1H, *J* = 12.93 Hz, 6.98 Hz, CH*H*CH=CH_2), 2.64–2.70 (dd, 1H, *J* = 12.80 Hz, 4.78 Hz, NCH*H*CH), 2.77–2.82 (dd, 1H, *J* = 12.93 Hz, 5.17 Hz, NC*H*HCH), 2.77–2.82 (dd, 1H, *J* = 12.93 Hz, 6.98 Hz, C*H*HCH=CH_2), 2.98–3.02 (dd, 1H, *J* = 6.09 Hz, 5.43 Hz, NC*H*), 3.40–3.50 (m, 2H, $[CH_3CH_2O)_2]$, 3.56–3.65 [m, 3H, $(CH_3CH_2O)_2$, NCH*H*Ar], 3.78 (d, 1H, *J* = 14.74 Hz, NC*H*HAr), 4.50 [t, 1H, *J* = 5.04 Hz, C*H*$(OEt)_2$], 4.87–4.96 (m, 2H, NCHCH_2CH=CH_2), 5.05–5.12 (m, 2H, HOCCH_2CH=CH_2), 5.80 (s, 2H, OCH_2O), 5.80–5.91 (m, 2H, 2 × C*H*=CH_2), 6.38 (s, 1H, Ar-H), 6.92 (s, 1H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.1, 15.2 [$(CH_3CH_2O)_2$], 28.3 (NCHCH_2CH=CH_2), 47.4 (HOCCH_2CH=CH_2), 50.7 (NCH_2Ar), 58.4 [NCH_2CH$(OEt)_2$], 61.8, 61.9 [$(CH_3CH_2O)_2$], 64.6 (NCH), 75.3 (HOCAr), 100.6 (OCH_2O), 102.0 [CH$(OEt)_2$], 105.0, 106.1, 126.9, 133.5, 146.2, 146.3 (Ar), 115.7 (NCHCH_2CH=CH_2), 119.0 (HOCCH_2CH=CH_2), 134.2 (HOCCH_2 CH=CH_2), 138.7 (NCHCH_2CH=CH_2); IR ($CHCl_3$): 1/λ = 3019 (s), 2977 (m), 2896 (w), 1637 (w), 1503 (w), 1483 (m), 1433 (w), 1390 (w), 1216 (s), 1127 (w), 1042 (m), 929 (w) cm^{-1}; MS (EI, 80 eV, 80–100 °C): *m/z* (%) = 389 (0.4, $[M]^+$), 348 (100, $[M - C_3H_5]^+$), 307 (53, $[M - C_6H_{10}]^+$), 245 (23, $[M - C_8H_{16}O_2]^+$), 204 (25, $[M - C_{11}H_{21}O_2]^+$), 103 (20, $[C_5H_{11}O_2]^+$); HRMS (80 eV, 100 °C): calcd. for $C_{19}H_{26}NO_5$ ($[M-C_3H_5]^+$): 348.18110; found: 348.18123.

Z-(3*R*)-3-Allyl-4-allylidene-*N*-(2,2-diethoxyethyl)-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline (24)

Under argon, allylisoquinoline **23** (100 mg, 0.25 mmol) in anhydrous DMSO (10 mL) was treated with MsCl (35 mg, 0.30 mmol) and *t*-BuOK (34 mg, 0.30 mmol). The mixture was stirred at 20 °C for 2 days. H_2O (10 mL) and Et_2O (10 mL) were added. The aqueous layer was extracted with Et_2O (4 × 10 mL), and the combined organic layers were dried over $MgSO_4$. After removal of the solvent under vacuum, the crude material was purified by column chromatography (*n*-hexane/ethyl acetate, 5:1) to give butadiene **24** as a brown oil which easily tended to decompose; yield: 37 mg (38%); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.13 [2 × t, 6H, *J* = 6.83 Hz, $(CH_3CH_2O)_2$], 2.01–2.15 (m, 1H, CH*H*CH=CH_2), 2.29–2.42 (m, 1H, C*H*HCH=CH_2), 2.51–2.57 (dd, 1H, *J* = 13.67 Hz, 4.88 Hz, NCH*H*CH), 2.58–2.65 (dd, 1H, *J* = 13.67 Hz, 5.38 Hz, NC*H*HCH), 3.38–3.50 (m, 2H, CH_3CH_2O), 3.53–3.65 (m, 3H, CH_3CH_2O, NCH*H*Ar), 3.93–3.98 (dd, 1H, *J* = 7.81 Hz, 7.32 Hz, NC*H*), 4.01 (d, 1H, *J* = 17.09 Hz, NC*H*HAr), 4.51–4.59 [dd, 1H, *J* = 5.37 Hz, 4.88 Hz, C*H*$(OEt)_2$], 4.88–4.98 (m, 2H, CH_2CH=CH_2), 5.06–5.10 (dd, 1H, *J* = 9.77 Hz, 1.95 Hz, C=CHCH=CH*H*), 5.21–5.26 (dd, 1H, *J* = 16.11 Hz, 1.95 Hz, C=CHCH=C*H*H), 5.70–5.80 (dddd, 1H, *J* = 17.09 Hz, 9.77 Hz, 7.32 Hz, 6.84 Hz, CH_2C*H*=CH_2), 5.81 (s, 2H, OCH_2O), 6.38 (s, 1H, Ar-H), 6.45 (d, 1H, *J* = 11.23 Hz, C=C*H*CH=CH_2), 6.54–6.63 (ddd, 1H, *J* = 16.11 Hz, 11.23 Hz, 9.77 Hz, C=CHC*H*=CH_2), 6.99 (s, 1H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.2 [$(CH_3CH_2O)_2$], 34.7 (CH_2CH=CH_2), 49.9 (NCH_2Ar), 57.3 (NCH_2CH), 58.4 (NCH), 61.8, 62.0 [$(CH_3CH_2O)_2$], 100.7 (OCH_2O), 102.5 [CH$(OEt)_2$], 103.4, 106.0, 127.3, 133.9, 135.7, 146.7, 147.3 (Ar), 116.0 (CH_2CH=CH_2), 117.7 (C=CHCH=CH_2), 123.2 (C=CHCH=CH_2), 126.0 (C=CHCH=CH_2), 132.5 (C=CHCH=CH_2), 135.7 (CH_2CH=CH_2); IR ($CHCl_3$): 1/λ = 3076 (m), 3018 (s), 2978 (s), 2933 (s), 2897 (s), 2775 (w) 1639 (m), 1616 (m), 1504 (s), 1481 (s), 1444 (m), 1375 (m), 1332 (m), 1231 (s), 1217 (s), 1175 (m), 1126 (m), 1042 (s), 987 (m) cm^{-1}; MS (EI, 80 eV, 100 °C): *m/z* (%) = 330 (100, [M –

$C_3H_5]^+$), 284 (15, $[M - C_4H_7O_2]^+$), 268 (16, $[M - C_5H_{11}O_2]^+$), 212 (41, $[M - C_9H_{19}O_2]^+$), 103 (13, $[C_5H_{11}O_2]^+$), 75 (14, $[C_3H_7O_2]^+$), 41 (12, $[C_3H_5]^+$).

(4a*R*,10b*R*)-*N*-(2,2-Diethoxyethyl)-8,9-methylenedioxy-1,4,4a,5,6,10b-hexahydrophenanthridine (25)

Diallylisoquinoline **23** (100 mg, 0.25 mmol) in CH_2Cl_2 (50 mL) was treated with benzylidenebis(tricyclohexylphosphine)dichlororuthenium (Grubbs' catalyst, 10 mg, 0.012 mmol). The mixture was refluxed at 60 °C. Another portion of Grubbs' catalyst (10 mg, 0.012 mmol) was added every 24 hours. After 96 hours, the reaction mixture was stirred at room temperature for 2 hours. The mixture was filtered over silica gel and the solvent was evaporated. The residue was purified by HPLC (ethyl acetate/*n*-hexane, 1:1, Nucleosil 50–5, 32 × 110 mm, flow 64 mL/min, retention time: 5.0 min) to give phenanthridine **25** as a brownish oil; yield: 60 mg (66%); $[\alpha]_D^{20}$: −144.5° (*c* 1.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.15 (2 × t, 6H, *J* = 7.01 Hz, C*H*$_3$CH$_2$), 2.10–2.20 (m, 2H, CH*H*CHN, CH*H*COH), 2.34–2.42 (m, 1H, C*H*HCHN), 2.51–2.57 [dd, 1H, *J* = 13.88 Hz, 4.81 Hz, NC*H*HCH(OEt)$_2$], 2.67–2.73 (dd, 1H, *J* = 10.76 Hz, 5.50 Hz, NC*H*), 2.78–2.85 (m, 1H, C*H*HCOH), 2.86 (s, br, 1H, O*H*), 3.02–3.08 [dd, 1H, *J* = 13.88 Hz, 5.67 Hz, NCH*H*CH-(OEt)$_2$], 3.48–3.56 (m, 2H, CH$_3$C*H*$_2$), 3.56–3.61 (d, 1H, *J* = 14.85 Hz, NC*H*HAr), 3.62–3.74 (m, 2H, CH$_3$C*H*$_2$), 3.91–3.97 (d, 1H, *J* = 14.99 Hz, NCH*H*Ar), 4.62–4.66 [dd, 1H, *J* = 5.49 Hz, 5.09 Hz, C*H*(OEt)$_2$], 5.63–5.68 (m, 1H, CH=C*H*CH$_2$COH), 5.69–5.75 (m, 1H, CH=C*H*-CHN), 5.88 (d, 2H, *J* = 1.37 Hz, OC*H*$_2$O), 6.39 (s, 1H, Ar-H), 6.89 (s, 1H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.31, 15.32 (*C*H$_3$CH$_2$), 26.4 (*C*H$_2$CHN), 35.8 (*C*H$_2$COH), 53.5 [N*C*H$_2$CH(OEt)$_2$], 56.3 (N*C*H$_2$Ar), 61.4 (CH$_3$*C*H$_2$), 61.6 (CH$_2$*C*HN), 62.4 (CH$_3$*C*H$_2$), 68.1 (*C*OH), 100.7 (O*C*H$_2$O), 101.4 [*C*H(OEt)$_2$], 105.3, 105.5, 127.4, 133.7, 146.5, 146.6 (Ar), 123.5 (CH=*C*HCH$_2$COH), 124.2 (CH=*C*HCH$_2$CHN); IR ($CHCl_3$): 1/λ = 3320 (w, OH), 3019 (s), 2978 (m), 2897 (m), 1605 (w), 1504 (m), 1486 (m), 1389 (w), 1294 (w), 1215 (s), 1126 (m), 1043 (m), 909 (s) cm^{-1}; MS (EI, 80 eV, 120 °C): *m/z* (%) = 361 (1.37, $[M]^+$), 343 (9, $[M - H_2O]^+$), 316 (6, $[M - C_2H_5O]^+$), 258 (100, $[M - C_5H_{11}O_2]^+$), 103 (7, $[C_5H_{11}O_2]^+$); HRMS (80 eV, 100 °C): calcd. for $C_{20}H_{27}NO_5$: 361.18892; found: 361.18744; calcd. for $C_{20}H_{25}NO_4$ ($[M - H_2O]^+$): 343.17835; found: 343.17654; calcd. for $C_{18}H_{22}NO_4$ ($[M - C_2H_5O]^+$): 316.15488; found: 316.15622; calcd. for $C_{15}H_{16}NO_3$ ($[M - C_5H_{11}O_2]^+$): 258.11301; found: 258.11633.

(3*R*)-*N*-(2,2-Diethoxyethyl)-8,9-methylenedioxy-4,4a,5,6-tetrahydrophenanthridine (26)

Under argon, phenanthridine **25** (100 mg, 0.27 mmol) in anhydrous DMSO (10 mL) was treated with MsCl (35 mg, 0.30 mmol) and *t*-BuOK (34 mg, 0.30 mmol). The mixture was stirred at 20 °C for 2 days. H_2O (10 mL) and Et_2O (10 mL) were added, the aqueous layer was extracted with Et_2O (4 × 10 mL), and the combined organic layers were dried over $MgSO_4$. After removal of the solvent in vacuum, the crude material was purified by column chromatography (*n*-hexane/ethyl acetate, 1:1) to afford cyclohexadiene **26** as a brown oil, which easily tended to decompose; yield: 20 mg (21%); $[\alpha]_D^{20}$: +162.9° (*c* 0.47, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.15 (2 × t, 6H, *J* = 7.33 Hz, C*H*$_3$CH$_2$), 2.11–2.28 (m, 1H, C*H*HCHN), 2.44–2.57 (m,1H, CH*H*CHN), 2.61–2.69 [dd, 1H, *J* = 14.16 Hz, 5.37 Hz, NC*H*H CH(OEt)$_2$], 2.69–2.77 [dd, 1H, *J* = 14.16 Hz, 4.88 Hz, NCH*H*CH(OEt)$_2$], 3.40–3.50 (m, 2H, CH$_3$C*H*$_2$), 3.53–3.65 (m, 2H, CH$_3$C*H*$_2$), 3.65–3.78 (d, 1H, *J* = 15.63 Hz, NC*H*HAr), 3.83–3.92 (d, 1H, *J* = 15.13 Hz, NCH*H*Ar), 4.52–4.59 [dd, 1H, *J* = 5.37 Hz, 4.88 Hz, C*H*(OEt)$_2$], 5.82 (2 × s, 2H, OC*H*$_2$O), 5.80–5.88 (m, 1H, CH$_2$C*H*=CH), 5.95–6.02 (m, 1H, CH=C*H*CH=C), 6.02–6.24 (m, 1H, CH=CHC*H*=C), 6,43 (s, 1H, C*H*CCH$_2$N), 6.97 (s, 1H, C*H*CC=CH); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.2 (*C*H$_3$CH$_2$), 28.2 (*C*H$_2$CHN), 53.6 [N*C*H$_2$CH(OEt)$_2$], 56.2 (N*C*H$_2$Ar), 59.9 (N*C*H), 61.8, 62.0 (CH$_3$*C*H$_2$), 100.6 (O*C*H$_2$O), 102.0 [*C*H(OEt)$_2$], 102.4, 106.7, 128.9, 132.9, 146.8, 146.9 (Ar), 115.7 (CH$_2$*C*H=CH), 124.7 (CH=CH*C*H=C), 125.7 (CH=*C*HCH=C), 126.3 (CH=*C*); IR ($CHCl_3$): 1/λ = 3019 (s), 2977 (m), 2928 (m), 2897 (m), 2413 (w), 1602 (w), 1503 (m), 1481 (s), 1377 (w), 1215 (s), 1122 (m), 1043 (m), 939 (m) cm^{-1}; MS (EI, 80 eV, 100 °C): *m/z* (%) = 343 (100, $[M]^+$), 298 (8, $[M - C_2H_5O]^+$), 240 (25, $[M - C_5H_{11}O_2]^+$), 211 (30, $[M - C_6H_{14}NO_2]^+$), 181 (60, $[M - C_7H_{14}O_4]^+$), 103 (35, $[C_5H_{11}O_2]^+$), 75 (25, $[C_3H_7O_2]^+$); HRMS (80 eV, 100 °C): calcd. for $C_{20}H_{25}NO_4$: 343.17835; found: 343.17654.

(5*R*,9*R*)-3,4-Diallyl-2,4-(2-ethoxy-3-oxapropylidine)-6,7-methylenedioxyisoquinoline (27)

Method A: Under argon, diallylisoquinoline **23** (200 mg, 0.51 mmol) was dissolved in anhydrous $CHCl_3$ (30 mL) and $SmCl_3$ (5 mg) and acetyl chloride (140 μL) were added at room temperature. The reaction mixture was stirred for 30 min. (TLC monitoring) at room temperature. NaOH (1 M) was added until the pH reached 9–10 and the aqueous layer was extracted with $CHCl_3$ (4 × 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed. The residue was purified by column chromatography (*n*-hexane/ethyl acetate, 3:1) to give acetal **27** as a yellow oil; yield: 150 mg (85%).

Method B: Diallylisoquinoline **23** (200 mg, 0.51 mmol) was treated with aqueous HCl (1 M, 20 mL). The reaction mixture was heated to 50 °C for 20 hours. NaOH (1 M) was added until the pH reached 9–10 and the aqueous layer was extracted with $CHCl_3$ (4 × 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed. The residue was purified by column chromatography (*n*-hexane/ethyl acetate, 3:1) to give acetal **27** as a yellow oil; yield: 110 mg (62%); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.05 (t, 3H, *J* = 7.33 Hz, C*H*$_3$CH$_2$), 2.40–2.60 (m, 3H, C*H*HCAr, C*H*HCHN, NC*H*HCH), 2.70–2.92 (m, 4H, CH$_2$C*H*N, CH*H*CAr, CH*H*CHN, NCH*H*CH), 3.12–3.26 (m, 1H, CH$_3$C*H*H), 3.64–3.76 (m, 1H, CH$_3$CH*H*), 3.77–3.85 (d, 1H, *J* = 17.58 Hz, NC*H*HAr), 4.23–4.30 (m, 2H, NCH$_2$C*H*(OEt), NCH*H*Ar), 4.91–5.15 (m, 4H, C*H*$_2$=CHCH$_2$CHN, C*H*$_2$=CHCH$_2$CAr), 5.31–5.47 (m, 1H, CH$_2$=C*H*CH$_2$CAr), 5.72–5.88 (m, 1H, CH$_2$=C*H*CH$_2$N), 5.91 (s, 2H, OC*H*$_2$O), 6.42 (s, 1H, Ar-H), 6.92 (s, 1H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.0 (*C*H$_3$CH$_2$O), 29.8 (NCH*C*H$_2$CH=CH$_2$), 38.3 (ArC*C*H$_2$CH=CH$_2$), 50.5 (N*C*H$_2$Ar), 57.4 (N*C*H$_2$CH), 57.8 (CH$_3$*C*H$_2$), 64.3 (N*C*H), 71.9 (CH$_2$*C*Ar), 94.3

[$NCH_2CH(OEt)_2$], 100.8 (OCH_2O), 104.6, 105.9, 131.6, 131.7, 146.8, 147.0 (Ar), 115.9 ($NCHCH_2CH{=}CH_2$), 118.5 ($ArCCH_2CH{=}CH_2$), 128.3 ($ArCHCH_2CH{=}CH_2$), 138.7 ($NCHCH_2CH{=}CH_2$); IR ($CHCl_3$): $1/\lambda = 3079$ (m), 3017 (s), 2979 (s), 2932 (m), 2896 (m), 1713 (w), 1641 (m), 1504 (s), 1486 (s), 1454 (m), 1440 (m), 1380 (m), 1332 (m), 1310 (m), 1266 (m), 1243 (s), 1215 (s), 1163 (m), 1129 (m), 1105 (m), 1041 (s), 939 (m) cm^{-1}; MS (EI, 80 eV, 80 °C): *m/z* (%) = 343 (50, $[M]^+$), 284 (27, $[M - C_3H_7O]^+$), 269 (44, $[M - C_3H_6O_2]^+$), 228 (77, $[M - C_6H_{11}O_2]^+$), 202 (100, $[M - C_9H_{17}O]^+$).

(4a*R*,10b*R*)-4,10b-(2-Ethoxy-3-oxapropylidine)-8,9-methylenedioxy-1,4,4a,5,6,10b-hexahydrophenanthridine (28)

Acetal **27** (120 mg, 0.35 mmol) in CH_2Cl_2 (80 mL) was treated with benzylidenebis(tricyclohexylphosphine)dichlororuthenium (Grubbs' catalyst, 14 mg, 0.017 mmol), the mixture was refluxed at 60 °C. Another portion of Grubbs' carbene (14 mg, 0.017 mmol) was added every 24 hours. After 96 hours, the reaction mixture was stirred at room temperature for 2 hours. The mixture was filtered over silica gel and the solvent was evaporated. The residue was purified by HPLC (ethyl acetate/*n*-hexane, 3:1, Nucleosil 50–5, 32 × 110 mm, flow 64 mL/min, retention time: 5.0 min) to give phenanthridine **28** as brown crystals; yield: 75 mg (68%); mp 138–139 °C; $[\alpha]_D^{20}$: −49.1° (*c* 1.3, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ = 1.02 (t, 3H, *J* = 7.15 Hz, CH_3CH_2), 2.11–2.19 (m, 1H, CH=CHC*H*HCHN), 2.36–2.44 (m, 1H, CH=CHC*H*HCAr), 2.59–2.65 (dd, 1H, *J* = 14.57 Hz , 3.57 Hz, NC*H*HCHOEt), 2.75–2.84 (m, 2H, CH=CHCH*H*CHN, CH=CHCH*H*CAr), 2.94–2.99 (dd, 1H, *J* = 10.86 Hz, 6.19 Hz, NC*H*CH_2), 3.09–3.15 (dd, 1H, *J* = 14.57 Hz, 10.03 Hz, NCH*H*CHOEt), 3.18–3.25 (m, 1H, CH_3CH*H*), 3.71–3.77 (m, 1H, CH_3CH*H*), 3.81–3.87 (d, 1H, *J* = 17.05 Hz, NC*H*HAr), 4.24–4.35 (d, 1H, *J* = 17.05 Hz, NCH*H*Ar), 4.33–4.37 (dd, 1H, *J* = 10.05 Hz, 3.71 Hz, EtOC*H*O), 5.50–5.60 (m, 1H, CH=C*H*CH_2CAr), 5.65–5.75 (m, 1H, CH=C*H*CH_2CHN), 5.90 (s, 2H, OCH_2O), 6.42 (s, 1H, Ar), 6.85 (s, 1H, Ar); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.0 (CH_3CH_2), 24.7 (NCHCH_2), 36.3 (CH=CHCH_2CAr), 51.1 (NCH_2CH), 54.6 (NCHCH$_2$), 57.7 (NCH_2Ar), 64.3 (CH_3CH_2), 67.4 (OCAr), 95.2 (NCH$_2$CHOEt), 100.8 (OCH_2O), 104.4, 105.4, 130.3, 131.0, 146.9, 147.0 (Ar), 122.9 (CH=CHCH$_2$CAr), 124.7 (CH=CHCH$_2$CHN); IR ($CHCl_3$): $1/\lambda = 3016$ (s), 2978 (s), 2928 (s), 2896 (s), 2775 (w), 2654 (w), 1665 (w), 1622 (w), 1504 (s), 1483 (s), 1450 (m), 1424 (m), 1380 (m), 1349 (m), 1333 (m), 1307 (m), 1260 (m), 1237 (s), 1214 (s), 1185 (m), 1161 (m), 1141 (m), 1111 (s), 1040 (s), 991 (w), 970 (w) cm^{-1}; MS (EI, 80 eV, 110 °C): *m/z* (%) = 315 (7, $[M]^+$), 270 (1, $[M - C_2H_5O]^+$), 241 (51, $[M - C_3H_6O_2]^+$), 226 (21, $[M - C_4H_9O_2]^+$), 212 (100, $[M - C_4H_9NO_2]^+$); HRMS (80 eV, 100 °C): calcd. for $C_{18}H_{21}NO_4$: 315.14705; found: 315.14932.

(2*R*)-2-[(*N*-*tert*-Butyloxycarbonyl)-*N*-(2,2-dimethoxyethyl)]amino-3,4-methylenedioxyphenyl-4-penten-1-one (29)

Under argon, 1-bromo-3,4-methylenedioxybenzene (110 μL, 0.91 mmol, *d* = 1.678, M_R = 201) in anhydrous THF (20 mL) was cooled to −78 °C. Butyllithium (360 μL, 0.90 mmol, 2.5 M in hexane) was injected dropwise. The mixture was stirred at −78 °C for 15 min. A solution of amide **18a** (400 mg, 0.80 mmol) in 5 mL anhydrous THF was added slowly. The mixture was stirred at −78 °C for a further 30 min (TLC monitoring). Saturated aqueous NH_4Cl (10 mL) was added to the mixture, the aqueous layer was extracted with Et_2O (4 × 10 mL), and the combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude material was purified by column chromatography (*n*-hexane/ethyl acetate, 5:1) to give ketone **29** as a yellow oil; yield: 220 mg (67.5%); $[\alpha]_D^{20}$: +110.7° (*c* 1.2, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$): δ = 1.40 [s, 9H, OC(CH_3)$_3$], 2.44–2.59 (m, 2H, $CH_2CH{=}CH_2$), 2.95, 3.06 (2 × s, 3H, OCH_3), 2.98–3.17 [m, 2H, $CH_2CH(OCH_3)_2$], 3.19, 3.27 (2 × s, 3H, OCH_3), 4.20–4.27, 4.37–4.45 [2 × dd, 1H, *J* = 4.88 Hz, 4.39 Hz, $CH(OCH_3)_2$], 4.92–4.98 (d, 1H, *J* = 11.23 Hz, CH=C*H*H), 5.01–5.09 (d, 1H, *J* = 17.09 Hz, CH=CH*H*), 5.43–5.52 (dd, 1H, *J* = 7.82 Hz, 6.83 Hz, C*H*CON), 5.61–5.84 (m, 1H, C*H*=CH_2), 5.94 (2 × s, 2H, OCH_2O), 6.71–6.79 (d, 1H, *J* = 8.30, Ar-H), 7.39–7.45 (d, 1H, *J* = 5.86 Hz, Ar-H), 7.50–7.67 (dd, 1H, *J* = 24.90 Hz, 8.30 Hz, Ar-H); ^{13}C NMR (68 MHz, $CDCl_3$): δ = 28.1 [OC(CH_3)$_3$], 32.8, 33.4 ($CH_2CH{=}CH_2$), 46.2, 48.0 [$CH_2CH(OCH_3)_2$], 54.3, 54.5, 54.6 (OCH_3), 58.2, 61.1 (*C*HCON), 80.6, 81.0 [O*C*(CH_3)$_3$], 101.5 (OCH_2O), 103.1, 103.5 [*C*H(OCH_3)$_2$], 107.6, 108.1, 124.1, 124.6, 130.7, 147.8, 151.4 (Ar), 117.3 (CH=CH_2), 134.2, 134.5 (*C*H=CH_2), 154.8, 155.4 (N*C*OO), 194.6, 195.3 (Ar*C*O); IR ($CHCl_3$): $1/\lambda = 3076$ (w), 2977 (m), 2932 (m), 1685 (s, CO, NCO), 1642 (w), 1605 (w), 1505 (m), 1489 (m), 1447 (s), 1402 (m), 1367 (m), 1305 (w), 1252 (s), 1166 (m), 1123 (m), 1075 (m), 1039 (m) cm^{-1}; MS (EI, 80 eV, 110 °C): m/z (%) = 407 (2, $[M]^+$), 334 (4, $[M - C_4H_9O]^+$), 276 (9, $[M - C_6H_{11}O_3]^+$), 258 (78, $[M - C_8H_5O_3]^+$), 202 (28, $[M - C_{12}H_{13}O_3]^+$), 158 (100, $[M - C_{13}H_{13}O_5]^+$); HRMS (80 eV, 110 °C): calcd. for $C_{21}H_{29}NO_7$: 407.19440; found: 407.19533.

(4*R*,5*R*)-4-(3,4-Methylenedioxyphenyl)-5-*N*-(*tert*-butyloxycarbonyl)-*N*-(2,2-dimethoxyethyl)amino-1,7-octadien-4-ol (30; crude material)

Under argon, allyltriphenyltin (210 mg, 0.53 mmol) was dissolved in anhydrous THF (10 mL). Phenyllithium (298 μL, 0.53 mmol, 1.8 M in cyclohexane/ether) was added. The mixture was stirred at 20 °C for 30 minutes, during this time a white precipitate occurred and the mixture changed from colourless to green. The so formed allyllithium was then cooled to −78 °C and ketone **29** (200 mg, 0.49 mmol) was injected dropwise. The mixture was stirred at −60 °C for a further 1 hour (TLC monitoring). Methanol (10 mL) was added and the solid was filtered off. The solvent was evaporated to give diallyl carbinol **30** as a yellow oil, which was used without further purification. ^1H NMR (270 MHz, $CDCl_3$): δ = 1.40 [2 × s, 9H, OC(CH_3)$_3$], 2.09 (m, 1H, O*H*), 2.25–2.90 (m, 4H, CHCH_2CH=CH_2, CCH_2CH=CH_2), 2.90–3.37 [m, 8H, NCH_2, CH(OCH_3)$_2$], 3.95–4.12 [2 × m, 1H, C*H*(OCH_3)$_3$], 4.21–4.35, 4.50–4.61 (2 × m, 1H, NC*H*), 4.76–5.11 (m, 4H, CHCH$_2$CH=CH_2, CCH$_2$CH=CH_2), 5.73–5.98 (m, 2H, CHCH$_2$C*H*=CH_2, CCH$_2$C*H*=CH_2), 6.81 (s, 2H, OCH_2O), 6.60–7.01 (m, 3H, Ar-H); ^{13}C NMR (68 MHz, $CDCl_3$): δ = 28.0 [OC(CH_3)$_3$], 30.9, 32.0 (CHCH_2CH=CH_2), 44.0, 45.7 (CCH_2CH=CH_2),

46.7, 46.9 [*C*H_2CH(OCH$_3$)$_2$], 53.8, 54.5 (OCH$_3$), 58.5, 60.4 (NCH), 78.8, 79.0 [OC(CH$_3$)$_3$], 79.7 (Ar*C*), 100.6 (O*C*H_2O), 104.0, 104.2 [*C*H(OCH$_3$)$_2$], 106.7, 106.9, 115.9, 116.9, 128.4, 128.9, 136.6, 137.0, 138.8, 139.1, 146.8, 147.3 (Ar), 117.2, 117.8 (CHCH$_2$CH=*C*H$_2$), 118.9, 119.1 (CCH$_2$CH=*C*H$_2$), 133.8, 134.9 (CHCH$_2$*C*H=CH$_2$), 136.6, 137.0 (CCH$_2$*C*H=CH$_2$), 156.3, 157.4 (N*C*O).

(4*R*,5*R*)-3-(2,2-Dimethoxyethyl)-4,5-diallyl-5-(3,4-methylenedioxyphenyl)-2-oxazolidinone (31)

Under argon, the crude carbinol **30** in anhydrous THF (20 mL) was treated with KHMDS (1.0 mL, 0.5 M in toluene) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min (TLC control). Saturated aqueous NH_4Cl (20 mL) was added to the mixture. The aqueous layer was extracted with Et_2O (4 × 10 mL). The combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude material was purified by column chromatography (*n*-hexane/ethyl acetate, 5:1) to give oxazolidinone **31** as a pale yellow oil; yield: 150 mg (81.4% from ketone 29); $[\alpha]_D^{20}$: +10.0° (*c*2.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.46–2.57 (m, 2H, CHC*H*$_2$CH=CH$_2$), 2.57–2.62 (dd, 1H, *J* = 14.43 Hz, 7.42 Hz, ArCC*H*H), 2.75–2.81 (dd, 1H, *J* = 14.44 Hz, 6.32 Hz, ArCCH*H*), 2.92–2.98 [dd, 1H, *J* = 14.71 Hz, 7.01 Hz, NC*H*HCH(OCH$_3$)$_2$], 3.01 (s, 3H, OC*H*$_3$), 3.21 (s, 3H, OC*H*$_3$), 3.54–3.59 [dd, 1H, *J* = 14.71 Hz, 3.99 Hz, NCH*H*CH(OCH$_3$)$_2$], 3.91–3.96 (dd, 1H, *J* = 6.46 Hz, 5.50 Hz, NC*H*), 4.10–4.14 [dd, 1H, *J* = 7.01 Hz, 3.99 Hz, C*H*(OCH$_3$)$_2$], 5.43–5.53 (dddd, 1H, *J* = 17.58 Hz, 10.26 Hz, 7.32 Hz, 6.35 Hz, ArCCH$_2$C*H*=CH$_2$), 5.73–5.82 (dddd, 1H, *J* = 17.09 Hz,10.17 Hz, 7.02 Hz, 6.88 Hz, NCHCH$_2$C*H*=CH$_2$), 5.90 (s, 2H, OC*H*$_2$O), 6.71–6.74 (d, 1H, *J* = 6.11 Hz, Ar-H), 6.75–6.80 (m, 2H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 33.0 (CH*C*H$_2$CH=CH$_2$), 39.6 (ArC*C*H$_2$CH=CH$_2$), 44.0 (*C*H$_2$CH(OCH$_3$)$_2$), 54.3, 55.1 (CH(OC*H*$_3$)$_2$), 65.9 (N*C*H), 84.9 (NCOO*C*), 101.0 (O*C*H$_2$O), 103.1 [*C*H(OCH$_3$)$_2$], 105.6, 107.9, 118.1, 136.9, 146.7, 147.7 (Ar), 118.8, 118.9 (CH=*C*H$_2$), 131.3 (ArCCH$_2$*C*H=CH$_2$), 133.2 (CHCH$_2$*C*H=CH$_2$), 156.7 (N*C*O); IR (film): 1/λ = 3086 (w), 3052 (w), 2992 (m), 2948 (s), 2898 (s), 2835 (m), 1732 (br, s, NCOO), 1635 (w), 1612 (m), 1507 (s), 1490 (s), 1438 (s), 1420 (s), 1392 (m), 1383 (m), 1357 (m), 1347 (m), 1316 (m), 1296 (m), 1283 (m), 1251 (s), 1210 (m), 1192 (m), 1178 (m), 1145 (m), 1121 (s), 1071 (s), 1035 (s), 1020 (s), 999 (m), 972 (m), 964 (m), 928 (m) cm^{-1}; MS (EI, 80 eV, 110 °C): *m/z* (%) = 375 (13.9, $[M]^+$), 344 (4, $[M - CH_3O]^+$), 334 (14, $[M - C_3H_5]^+$), 315 (10, $[M - C_2H_4O_2]^+$), 293 (3, $[M - C_6H_{10}]^+$), 274 (4, $[M - C_5H_9O_2]^+$), 258 (23, $[M - C_5H_9O_3]^+$), 228 (7, $[M - C_6H_{11}O_4]^+$), 75 (100, $C_3H_7O_2$); HRMS (80 eV, 110 °C): calcd. for $C_{20}H_{25}O_6N$: 375.16818; found: 375.16911.

(3a*R*,7a*R*)-3-(2,2-Dimethoxyethyl)-7a-(3,4-methylenedioxyphenyl)-3a,4,7,7a-tetrahydrobenzooxazol-2-one (32)

Oxazolidinone **31** (100 mg, 0.27 mmol) in CH_2Cl_2 (80 mL) was treated with benzylidenebis(tricyclohexylphosphine)dichlororuthenium (Grubbs' catalyst, 11 mg, 0.013 mmol). The reaction mixture was refluxed at 60 °C for 3 hours (TLC control). After removal of the solvent, the residue was purified by column chromatograph (*n*-hexane/ethyl acetate, 3:1) to give cyclohexene **32** as a pale yellow oil; yield: 80 mg (86%); $[\alpha]_D^{20}$: −37.3° (*c* 1.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.17–2.25 (m, 1H, NCHC*H*H), 2.36–2.43 (m, 1H, ArCC*H*H), 2.48–2.53 (ddd, 1H, *J* = 15.63 Hz, 5.37 Hz, 2.93 Hz, NCHCH*H*), 2.58–2.65 (dd, 1H, *J* = 16.60 Hz, 5.86 Hz, ArCCH*H*), 2.91–2.96 (dd, 1H, *J* = 14.65 Hz, 6.35 Hz, NC*H*H), 3.21 (s, 3H, OC*H*$_3$), 3.32 (s, 3H, OC*H*$_3$), 3.51–3.56 (dd, 1H, *J* = 14.65 Hz, 4.39 Hz, NCH*H*), 4.07–4.12 (dd, 1H, *J* = 4.89 Hz, 2.93 Hz, NC*H*), 4.33–4.38 [dd, 1H, *J* = 5.86 Hz, 4.40 Hz, C*H*(OCH$_3$)$_2$], 5.89–5.93 (m, 1H, C*H*=CH), 5.92 (s, 2H, OC*H*$_2$O), 5.93–6.01 (m, 1H, CH=C*H*), 6.67–6.71 (d, 1H, *J* = 8.30 Hz, Ar-H), 6.78–6.83 (dd, 1H, *J* = 8.30 Hz, 1.96 Hz, Ar-H), 6.83–6.85 (d, 1H, *J* = 1.46 Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 25.6 (NCH*C*H$_2$), 36.0 (ArC*C*H$_2$), 43.5 (N*C*H$_2$), 54.4, 55.1 (O*C*H$_3$), 63.0 (N*C*HCH$_2$), 82.9 (NCOO*C*), 101.1 (O*C*H$_2$O), 102.9 [*C*H(OCH$_3$)$_2$], 105.0, 107.9, 117.2, 138.6, 147.0, 147.8 (Ar), 125.8 (*C*H=CH), 127.4 (CH=*C*H), 157.3 (N*C*O); IR (film): 1/λ = 3086 (w), 3052 (w), 2992 (w), 2948 (m), 2898 (m), 2835 (m), 1847 (w), 1732 (s, CON), 1635 (w), 1612 (w), 1507 (s), 1490 (s), 1438 (s), 1420 (s), 1392 (m), 1383 (m), 1357 (m), 1347 (m), 1326 (m), 1316 (m), 1296 (s), 1283 (m), 1251 (s), 1210 (m), 1192 (m), 1178 (m), 1145 (m), 1121 (m), 1071 (s), 1035 (s), 1020 (s), 999 (m), 972 (m), 964 (m), 928 (s) cm^{-1}; MS (EI, 80 eV, 120 °C): *m/z* (%) = 347 (8, $[M]^+$), 200 (8, $[C_{13}H_{12}O_2]^+$), 75 (100, $[C_3H_7O_2]^+$); HRMS (80 eV, 120 °C): calcd. for $C_{18}H_{21}NO_6$: 347.13690; found: 347.13588.

(4*R*,5*R*)-4-(3,4-Methylenedioxyphenyl)-5-(4-methoxy-2-oxazolidinonyl)-1,7-octadien-4-ol (33)

Method A: Crude diallyl carbinol **30** (150 mg, 0.33 mmol) in DMSO (30 mL) and H_2O (1 mL) was heated to 80–90 °C for 20 hours. The mixture was then cooled to room temperature and H_2O (10 mL) was added. The aqueous layer was extracted with Et_2O (4 × 10 mL), and the combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude material was purified by column chromatography (*n*-hexane/ethyl acetate, 2:1) to give methoxyoxazolidinone **33** as a yellow oil; yield: 90 mg (74% from ketone **29**).

Method B: Under argon, the crude diallyl carbinol **30** (150 mg, 0.33 mmol) in anhydrous $CHCl_3$ (20 mL) was treated with cat. $SmCl_3$ and acetyl chloride (90 μL) at room temperature. The reaction mixture was stirred for 30 min (TLC monitoring). Saturated aqueous $NaHCO_3$ (20 mL) was added until the pH reached 9–10 and the aqueous layer was extracted with $CHCl_3$ (4 × 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed. The residue was purified by column chromatography (*n*-hexane/ethyl acetate, 2:1) to give methoxyoxazolidinone **33** as a yellow oil; yield: 80 mg (66% from ketone **29**).

Method C: Crude diallyl carbinol **30** (150 mg, 0.33 mmol) in anhydrous CH_3OH (30 mL) at 0 °C was treated with $SOCl_2$ (1 mL). The mixture was stirred at 0 °C for 3 hours. After removal of the solvent, Na_2CO_3 (10 mL) was added. The aqueous layer was extracted with Et_2O (4 × 10 mL), and the combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude material was purified by column chromatography (*n*-hexane/ethyl acetate, 2:1) to give methoxyoxazolidinone **33** as a yellow oil; 70 mg (58% from ketone **29**). The me-

thoxyoxazolidinone 33 was obtained as an inseparable mixture of diastereomers.

Data obtained from the mixture, separated peaks of diastereomer 1: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.39–2.70 (m, 4H, 2 × CH_2CH=CH_2), 3.02–3.08 (dd, 1H, *J* = 10.59 Hz, 3.02 Hz, NC*H*H), 3.29 (s, 3H, OCH_3), 3.49–3.54 (dd, 1H, *J* = 10.59 Hz, 6.60 Hz, NCH*H*), 3.80–3.90 (m, 1H, NC*H*), 4.93–5.09 (m, 5H, 2 × CH=CH_2, C*H*OCH_3), 5.22–5.30 (m, 1H, ArCCH$_2$C*H*=CH_2), 5.60–5.71 (m, 1H, NCHCH$_2$C*H*=CH_2), 5.82 (2 × s, 2H, OCH_2O), 6.62–6.67 (d, 1H, *J* = 1.46 Hz, Ar-H), 6.73–6.78 (dd, 1H, *J* = 8.31 Hz, 1.96 Hz, Ar-H), 6.80–6.84 (d, 1H, *J* = 7.81 Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 30.4 (NCH*C*H$_2$), 44.4 (ArC*C*H$_2$CH=CH$_2$), 55.4 (O*C*H$_3$), 61.0 (N*C*H), 78.4 (Ar*C*), 98.4 (O*C*HOCH$_3$), 100.8 (O*C*H$_2$O), 106.8, 107.7, 120.1, 137.6, 146.4, 147.7 (Ar), 118.2 (CH=*C*H$_2$), 118.9 (CH=*C*H$_2$), 132.6 (*C*H=CH$_2$), 134.5 (*C*H=CH$_2$), 157.5 (*C*ON).

Data obtained from the mixture, separated peaks of diastereomer 2: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.39–2.70 (m, 4H, 2 × CH_2CH=CH_2), 3.22–3.28 (dd, 1H, *J* = 10.17 Hz, 2.20 Hz, NC*H*H), 3.22–3.28 (m, 4H, OCH_3, NCH*H*), 3.90–4.00 (m, 1H, NC*H*), 4.93–5.09 (m, 5H, 2 × CH=CH_2, C*H*OCH_3), 5.30–5.39 (m, 1H, ArCCH$_2$C*H*=CH_2), 5.60–5.71 (m, 1H, NCHCH$_2$C*H*=CH_2), 5.82 (2 × s, 2H, OCH_2O), 6.62–6.67 (d, 1H, *J* = 1.46 Hz, Ar-H), 6.73–6.78 (dd, 1H, *J* = 8.31 Hz, 1.96 Hz, Ar-H), 6.80–6.84 (d, 1H, *J* = 7.81 Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 30.4 (NCH*C*H$_2$), 45.0 (ArC*C*H$_2$CH=CH$_2$), 55.7 (O*C*H$_3$), 61.5 (N*C*H), 78.3 (Ar*C*), 98.6 (O*C*HOCH$_3$), 100.8 (O*C*H$_2$O), 106.1, 107.8, 120.3, 137.3, 146.5, 147.6 (Ar), 117.6 (CH=*C*H$_2$), 118.3 (CH=*C*H$_2$), 132.3 (*C*H=CH$_2$), 134.0 (*C*H=CH$_2$), 156.8 (CON).

Data of diastereomers 1 and 2: IR (film): 1/λ =3423 (br, m, OH), 3077 (m), 3005 (m), 2977 (m), 2957 (m), 2938 (m), 2843 (w), 2777 (w), 2249 (w), 1734 (s, CON), 1640 (m), 1610 (w), 1504 (s), 1488 (s), 1433 (s), 1377 (s), 1335 (m), 1238 (s), 1183 (m), 1125 (m), 1074 (m), 1040 (s), 1017 (m), 971 (m), 915 (m) cm^{-1}; MS (EI, 80 eV, 150 °C): *m/z* (%) = 361 (8, $[M]^+$), 343 (1, $[M - H_2O]^+$), 330 (2, $[M - CH_3O]^+$), 288 (2, $[M - C_3H_5O_2]^+$), 191 (47, $[M - C_8H_{10}O_4]^+$), 149 (100, $[C_8H_5O_3]^+$), 121 (6, $[C_7H_5O_2]^+$); HRMS (80 eV, 150 °C): calcd. for $C_{19}H_{23}NO_6$: 361.15253; found: 361.15366.

(1*R*,6*R*)-1-(3,4-Methylenedioxyphenyl)-6-*N*-(4-methoxy-2-oxazolidinonyl)-3-cyclohexen-1-ol (34)

Methoxyoxazolidinone **33** (160 mg, 0.44 mmol) in CH_2Cl_2 (100 mL) was treated with benzylidenebis(tricyclohexylphosphine)dichlororuthenium (Grubbs' catalyst, 16 mg, 0.022 mmol). The reaction mixture was refluxed at 60 °C for 3 hours (TLC control). After removal of the solvent, the residue was purified by column chromatography (ethyl acetate) to give cyclohexene **34** as colourless crystals; yield: 130 mg (88%); mp 188–189 °C. Cyclohexene 34 was obtained as an inseparable mixture of diastereomers.

Data obtained from the mixture, separated peaks of diastereomer 1: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.13–2.36 (m, 2H, NCHC*H*H, ArCC*H*H), 2.48–2.63 (m, 2H, NCHCH*H*, ArCCH*H*), 3.18–3.25 (dd, 1H, *J* = 10.74 Hz, 2.44 Hz, NC*H*H), 3.37 (s, 3H, OCH_3), 3.50–3.56 (dd, 1H, *J* = 10.74 Hz, 6.34 Hz, NCH*H*), 4.29–4.37 (dd, 1H, *J* = 10.72 Hz, 5.91 Hz, NC*H*), 5.07–5.10 (dd, 1H, *J* = 6.46 Hz, 2.47 Hz, CH$_3$OC*H*O), 5.54–5.64 (m, 1H, ArCCH$_2$C*H*=CH), 5.72–5.82 (m, 1H, ArCCH$_2$CH=C*H*), 5.90 (s, 2H, OCH_2O), 6.75 (d, 1H, *J* = 7.81 Hz, Ar-H), 6.88–6.93 (dd, 1H, *J* = 8.31 Hz, 1.96 Hz, Ar-H), 7.01 (d, 1H, *J* = 1.46 Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 25.9 (NCH*C*H$_2$), 43.9 (ArC*C*H$_2$), 50.8 (N*C*H$_2$), 55.2 (N*C*H), 55.3 (O*C*H$_3$), 74.8 (Ar*C*CH$_2$), 98.4 (CH$_3$O*C*HO), 100.9 (O*C*H$_2$O), 105.9, 107.9, 118.0, 138.8, 146.5, 147.6 (Ar), 124.2 (ArCCH$_2$*C*H=CH), 125.7 (ArCCH$_2$CH=*C*H).

Data obtained from the mixture, separated peaks of diastereomer 2: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.13–2.36 (m, 2H, NCHC*H*H, ArCC*H*H), 2.48–2.60 (m, 1H, ArCCH*H*), 2.62–2.73 (m, 1H, NCHCH*H*), 3.32–3.36 (dd, 1H, *J* = 10.45 Hz, 2.61 Hz, NC*H*H), 3.29 (s, 3H, OCH_3), 3.41–3.49 (dd, 1H, *J* = 10.45 Hz, 6.35 Hz, NCH*H*), 4.01–4.07 (dd, 1H, *J* = 10.45 Hz, 5.37 Hz, NC*H*), 5.14–5.17 (dd, 1H, *J* = 6.32 Hz, 2.61 Hz, CH$_3$OC*H*O), 5.54–5.64 (m, 1H, ArCCH$_2$C*H*=CH), 5.72–5.82 (m, 1H, ArCCH$_2$CH=C*H*), 5.90 (s, 2H, OCH_2O), 6.77 (d, 1H, *J* = 8.31 Hz, Ar-H), 6.88–6.93 (dd, 1H, *J* = 8.31 Hz, 1.96 Hz, Ar-H), 7.01 (d, 1H, J = 1.96 Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 25.7 (NCH*C*H$_2$), 43.2 (ArC*C*H$_2$), 49.0 (N*C*H$_2$), 55.7 (O*C*H$_3$), 57.2 (N*C*H), 75.0 (Ar*C*CH$_2$), 98.4 (CH$_3$O*C*HO), 100.9 (O*C*H$_2$O), 106.3, 107.8, 118.2, 138.2, 146.5, 147.7 (Ar), 124.5 (ArCCH$_2$*C*H=CH), 125.1 (ArCCH$_2$CH=*C*H) ppm.

Data of diasteoromers 1 and 2: IR (film): 1/λ = 3375 (br, m, OH), 3073 (w), 3063 (w), 3031 (w), 3000 (w), 2962 (w), 2925 (w), 2904 m), 2836 (w), 1733 (s, CON), 1654 (w), 1612 (w), 1505 (s), 1483 (s), 1447 (s), 1424 (s), 1389 (s), 1364 (s9, 1347 (w), 1338 (w), 1329 (w), 1315 (w), 1271 (s), 1247 (s), 1236 (s), 1216 (s), 1192 (m), 1151 (w), 1133 (w), 1125 (w), 1112 (m), 1100 (w), 1091 (w), 1068 (w), 1047 (s), 1040 (s), 1020 (s), 977 (s) cm^{-1}; MS (EI, 80 eV, 150 °C): *m/z* (%) = 333 (37, $[M]^+$), 216 (26, $[M - C_4H_7NO_3]^+$), 149 (100, $[C_8H_5O_3]^+$), 121 (8, $[C_7H_5O_2]^+$). HRMS (80 eV, 150 °C): calcd. for $C_{17}H_{19}NO_6$: 333.12125; found: 333.12322.

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