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Synthesis of Optically Active *N*-Allyl Amino Compounds with Defined Trisubstituted Double Bonds

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Abstract: Optically active acyclic *N*-allylamino compounds with defined configurated trisubstituted double bonds were generated via a three step sequence. The first crucial step was a two-carbon chain elongation of chiral α-aminoacid esters succeeding in a Claisen ester condensation with acetic acid ester enolates. The so formed β-ketoesters were subjected to a one pot procedure of an enol trifluoromethanesulfonate generation and a consecutive palladium catalysed cross-coupling: A Stille or a Sonogashira type reaction allowed to generate selectively the trisubstituted *E*-olefins. © 1999 Elsevier Science Ltd. All rights reserved.

INTRODUCTION

The generation of optically active allylamines with a free or a protected nitrogen function and with defined trisubstituted double bonds in acyclic or alicyclic molecules is still a goal of synthetic efforts. On the one hand, such allylamine structures can be encountered as a part of a natural or pharmaceutically interesting product,[1] on the other hand the allylamines serve as key fragments in complicated syntheses to allow further defined transformations like redox reactions, alkylations or rearrangements.[2]

The synthesis of optically active allylamines can in principle be initiated via two different strategies: The first one can be described as the introduction of an amino group in an pre-formed allylic system (allylic substitution) generating the C-N bond as the key step.[3] The second type represents the introduction of an olefin adjacent to an amino group either by an addition of a vinyl anion to an imine[4] or by the constitution of the double bond via eliminations, enolisations or Wittig type processes.[5] However, the key step of the second strategy is characterised by the formation of a C-C bond as the key step.

The chiral information can originate from commercially available optically active amino acids. The decision in favour for an ex chiral pool synthesis raises the question for a suitable method to generate stereoselectively the trisubstituted double bond adjacent to the amino function. Wittig and Horner type olefinations are known to build up such olefins stereoselectively, but most of them are restricted to the introduction of a small third substituent like a methyl group (R'' in Figure 1).[6] In contrast, palladium(0) catalysed reactions are of significantly increased flexibility in respect of the third substituent generating acyclic olefin fragments,[7] but before

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hand a convenient chain elongation to introduce at least two additional carbon atoms bearing functional groups is required. Even though Pd(0) catalysed cross-couplings are extensively used in olefin syntheses,[8] until now, the generation of allylamines is still sparsely investigated. This paper reports on the short ex chiral pool synthesis of flexible functionalised acyclic allylamino compounds with defined configurated trisubstituted double bonds as shown in figure 1.

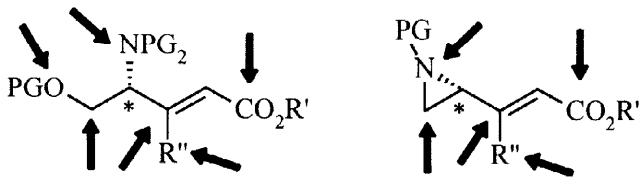


Fig. 1: Optically active acyclic *N*-allylamino compounds with defined trisubstituted olefins: defined but flexible transformations are possible in the arrow marked positions.
R' = Et, *i*Pr, R'' = Ar, C≡CTMS

RESULTS

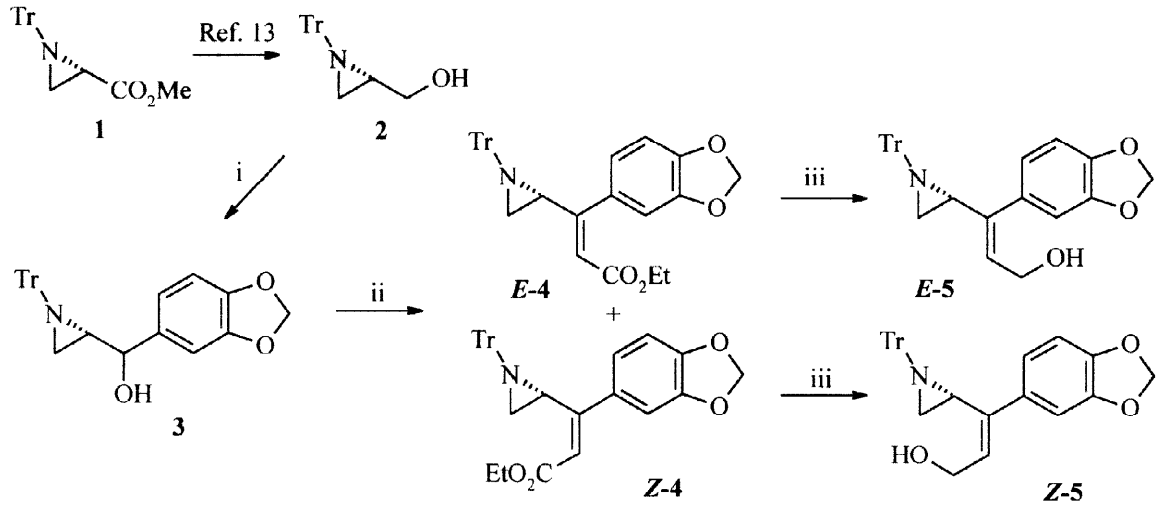
L-(-)-Serine represented a convenient starting material for ex chiral pool syntheses. In order to prepare the material for the chain elongation steps amino and hydroxyl function had to be suitably protected. In the first series the aziridinylester **1** bearing an electron rich N-function with a bulky N-trityl protective group was used as the key reactant. In the second series the investigations started with oxazolidinester **13** and the acyclic carbamate **18** involving acceptor substituted N-functions.

Vinylaziridines

Aziridinylester **1** was generated in three steps from *L*-(-)-serine according to literature procedures.[9] Initial investigations were focused on the Horner-Wadsworth-Emmons reaction[10] as the crucial olefination step to build up the trisubstituted double bond in order to test the stereoselectivity: Thus, aziridinylester **1** was reduced to the corresponding carbinol **2**.[11] A sequence of a Swern oxidation[12] and an aryllithium addition[13] to the intermediately generated aldehyde gave the alcohol **3** in 64 % as a mixture of diastereomers (about 1:1).

The separation of the compounds was unnecessary because a second Swern oxidation[12] destroyed the newly formed stereogenic centre. The resulting ketone was treated with an excess of sodium phosphonoacetate to give the α,β-unsaturated aminoesters **4** in about 60% yield. The isomers *E*-**4** (41%) and *Z*-**4** (17%) were separated by means of a column chromatography. The configurations of the trisubstituted olefins were proved via NOE analyses after DIBALH reduction[14] to the corresponding allylalcohols *E*-**5** (71% yield) and *Z*-**5** (68% yield), respectively.

The present sequence pointed out, that the attempt to introduce the trisubstituted double bond stereoselectively was dissatisfying employing the Horner reaction. Furthermore, five steps were necessary to convert the ester **1** into the desired allylamine *E*-**4**.



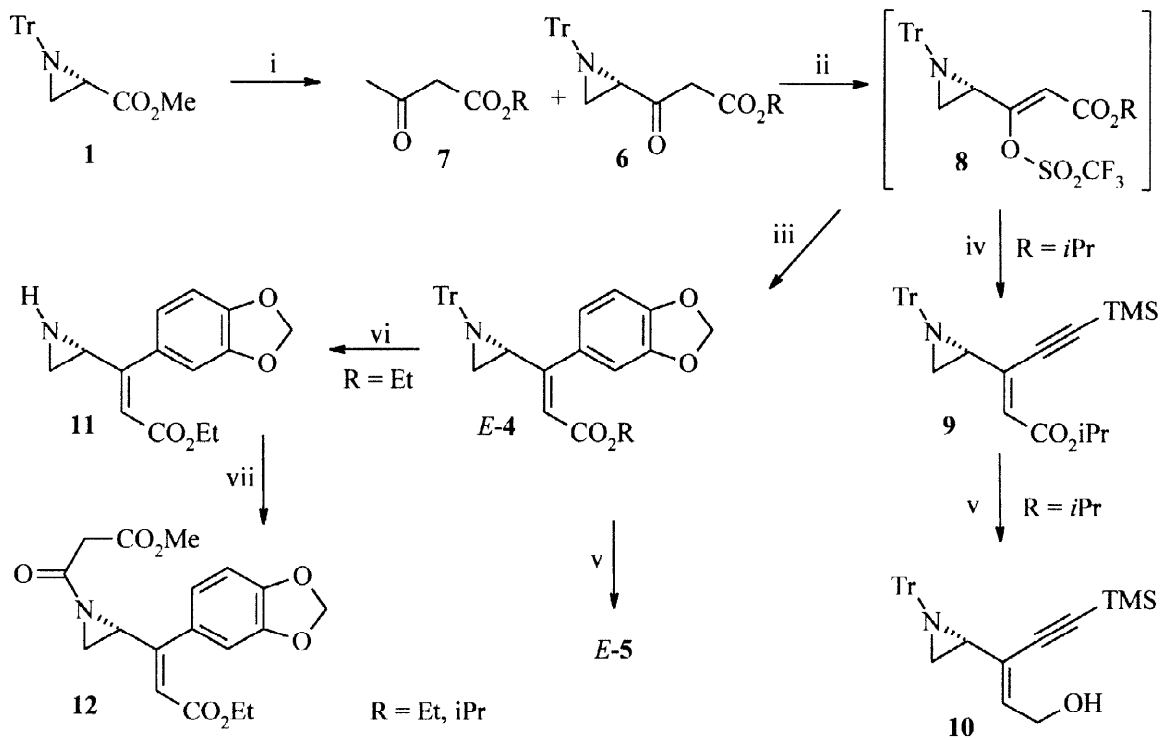
Scheme 1: Synthesis of vinylaziridines via Horner olefination:

i: 1. $C_2Cl_2O_2$, DMSO, Et_3N, CH_2Cl_2, -78→20°C, 3 h; 2. 3,4-Methylenedioxyphenyl-Li, THF, -78→20°C, 14 h. ii: 1. $C_2Cl_2O_2$, DMSO, Et_3N, CH_2Cl_2, -78→20°C, 3 h; 2. NaH/ $(EtO)_2P(O)CH_2CO_2Et$, THF, 20 °C, 2 d. iii: DIBALH, Et_2O, -20→20°C, 2 h.

β-Ketoesters had been described to as useful intermediates in the synthesis of α,β-unsaturated esters bearing trisubstituted olefins.[15] The shortest route to achieve the aziridinyl-β-ketoesters **6** starting from the aziridinylester **1** was a Claisen ester condensation with the enolate of an acetic acid alkylester.[16] Usually, such condensations should be carried out with acetic acid *t*butylester enolates to avoid any competing formation of acetoacetates **7** (self-condensation of the reagent). In the present case the synthesis of a potential β-keto-*t*butylester was thought to be disadvantageous: the chemoselective differentiation of an acid labile *t*butylester and the acid labile trityl group in projected products related to the aminoesters *E*-**4** and **9**, respectively, was expected to cause some difficulties. Thus, the β-ketoesters **6** (R = Et, *i*Pr) were synthesised by Claisen condensations of the aziridinylester **1** with acetic acid ethyl- or *i*propylester enolates, respectively, under carefully optimised reaction conditions (v. experimental part): Most of the competing acetoacetates **7** were observed to be formed, if the reaction temperature was not kept carefully at -78 °C. Usually, the separation of the acetoacetates **7** from the aminoesters **6** required the employment of preparative HPLC techniques. Considering the technical requirements, the β-ketoesters **6** were obtained in 70 % (R = Et) and 78 % (R = *i*Pr) yield.

The conversion of the β-ketoesters **6** into the α,β-unsaturated aziridinylesters *E*-**4** and **9** bearing an additional aryl or alkynyl substituent in a *cis*-position with respect to the ester group was achieved by Pd catalysed Stille[17] or Sonogashira[18] cross-coupling reactions, respectively. Initial experiments to activate the ketoesters as enolphosphates according to Weiler[19] failed because of their low reactivity. Hence the enoltriflates (enol trifluoromethanesulfonates) **8**[20] were generated *in situ* to guarantee an adequate leaving group quality during the cross-coupling reactions. After deprotonation of **6** with diisopropylamine in THF at -78 °C the corresponding

enoltriflates **8** were generated by addition of Tf_2O (trifluoromethanesulfonic acid anhydride). Without work-up the cross-coupling was carried out after dilution with dry *N*-methylpyrrolidone (NMP) by addition of the Pd(0)-catalyst, zinc chloride, triphenylarsane[21] and the piperonyl[22] or ethynyl stannane[23], respectively, to give the desired aminoesters *E*-**4** and **9** after 4 to 7 days of stirring at 20 °C. The low stability of the aziridinyl enoltriflates **8** necessitated to involve a one pot procedure of O-acylation and subsequent cross-coupling reaction building up *E*-**4** (R = Et: 23%, R = *i*Pr: 41%) and **9** (44%) to achieve preparatively useful yields over two steps.



Scheme 2. Synthesis of vinylaziridines via β-ketoester formation and cross-coupling reaction: i: H_3CCO_2R'/LDA, THF, -78 °C, 2 h, then **1** THF, -78 °C, 12 h. ii: iPr_2NH, THF, -78 °C, 15 min, then Tf_2O, THF, -78 °C, 2 h. iii: $Pd_2(dba_3)(CHCl_3)$ cat., Ph_3As, *N*-methylpyrrolidone, (3,4-methylenedioxyphenyl)-$SnBu_3$, $ZnCl_2$, Et_2O, -50→20°C, 4 to 6 d. iv: $Pd_2(dba_3)(CHCl_3)$ cat., Ph_3As, NMP, $TMSC{\equiv}CSnBu_3$, $ZnCl_2$, Et_2O, -50→20°C, 7 d. v: DIBALH, Et_2O, -20→20°C, 3 h. vi: HCO_2H, $CHCl_3$, MeOH, -20 °C, 6 h. vii: $ClC(O)CH_2CO_2CH_3$, Et_3N, THF, -20→20°C, 12 h.

Handling the aziridinyl systems it was mandatory to keep the reaction time as short as possible because of some side reactions: The aziridinyl systems *E*-**4** and **9** underwent partly aziridine ring openings with destruction of the stereogenic centre, the acetylene **9** suffered from a slow alkyne dimerisation under the reaction conditions. The configurations of the trisubstituted olefins were proved via NOE analyses after DIBALH re-

duction[14] of *E*-**4** (R = *i*Pr) to the corresponding allylalcohol *E*-**5** (71% yield) and of **9** to **10** (46% yield), respectively.

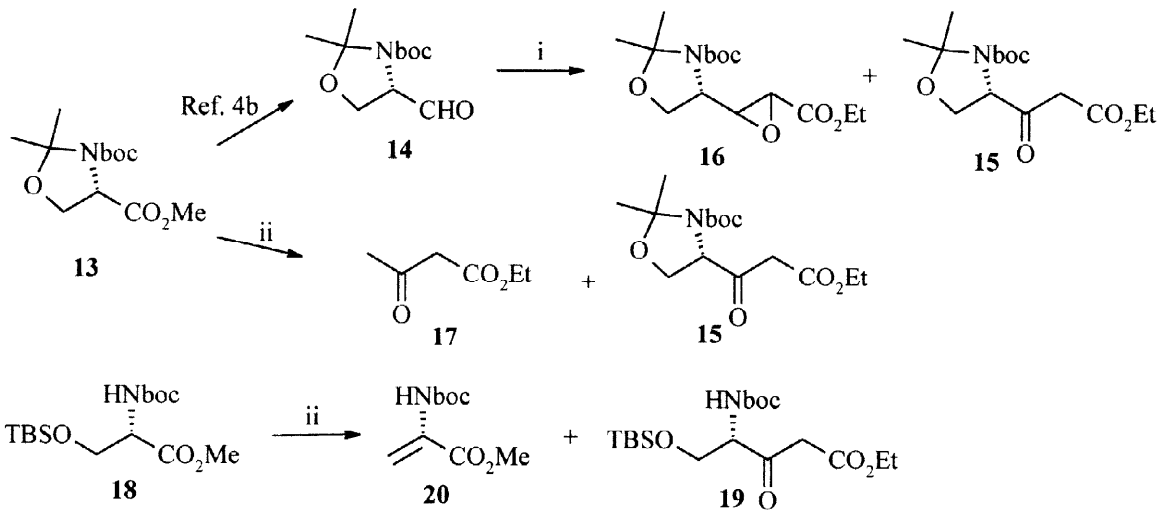
With the intention to employ the aziridinylesters in further syntheses of natural products the *N*-trityl protective group must be removable without affecting the potentially labile allylic unit. Hence, the aziridinylester *E*-**4** was treated with formic acid in $CHCl_3$ at low temperatures to remove the *N*-trityl group,[24] the deprotected aziridine **11** was isolated in 70% yield. Most of the variations of the reaction conditions (solvent, acid) led to the severe decrease of the yield. In most cases aziridin ring openings were observed to give either allylalcohols or β-eliminations to form α,β,γ,δ-unsaturated esters, pointing out, that any stronger acidic conditions especially in the presence of nucleophiles (e. g. MeOH) should be carefully avoided. It was found to be advantageous to protect the nitrogen of the crude aziridine as an amide: The treatment with malonic acid monomethylester chloride in presence of a weak base led to the formation of the corresponding malonamide **12** in 74% yield. Strong bases should be avoided to shield the product against aziridine ring openings or Michael additions. In conclusion, the aziridinyl amino group should serve as an useful anchoring point for further substituents.

N-boc-Allylamines

The synthesis of the vinylaziridines pointed out some limitations of the cross-coupling reactions adjacent to the sensitive three-membered heterocycle. With the intention to investigate some acceptor substituted *N*-boc amino compounds the oxazolidinester **13**[25] and the acyclic carbamate **18**[26] were generated in three steps from *L*-(-)-serine according to literature procedures. First efforts had been focused on an alternative synthesis of the β-ketoester **15**. In order to exclude any epimerisation of the stereogenic centre basic reaction conditions for the C-2 elongation were avoided: The aminoester **13** was transformed into the corresponding aldehyde **14** either via reduction/oxidation sequence[11] as described for the aziridinester **1** or with a direct DIBALH reduction at low temperatures.[25] Then, the aldehyde **14** was treated with ethyl diazoacetate in presence of a catalytic amount of $SnCl_2$ to give the desired **15** in 40 % yield and the glycidesters **16** (12 % yield) as a side product.[27] In the present case, two or three steps and the separation of a side product (→ **16**) via column chromatography were necessary to convert the ester **13** into the desired β-ketoester **15**.

The direct route to achieve the *N*-boc amino-β-ketoesters **15** and **19** starting from the *N*-boc aminoesters **13** and **18** was the Claisen ester condensation as described for the synthesis of aziridin ester **6**.[16] Thus, the reactants **13** and **18** were treated with the lithium enolate of ethyl acetate, respectively, under the carefully optimised reaction conditions as mentioned above (v. experimental part). The formation of the competing acetoacetate **17** should be suppressed as far as possible to avoid any intricate separation by preparative HPLC techniques. Considering the technical requirements, the β-ketoester **15** was obtained in 76% yield. Unfortunately, in most cases the yield of **19** was significantly lower (< 50 %) because of the preferential formation of the elimination product **20** (up to 35 %).[26d] The poor yield synthesising the acyclic β-ketoester **19** led to the abandon-

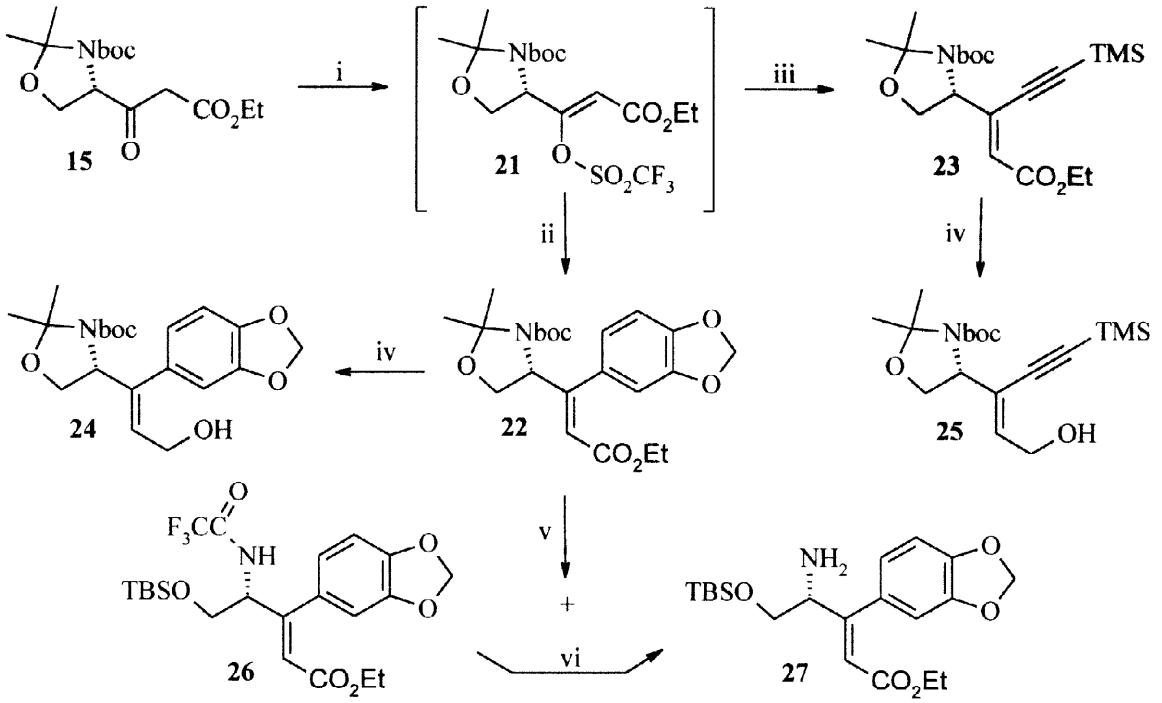
ment of that path, the desired *N*-boc allylamine should be easily achieved by the protection of the aminoester **27** (v. below). In summary, the Claisen condensation represented the most efficient method to generate the β-ketoester **15** starting from the cyclic *N*-boc aminoester **13** (1 step).



Scheme 3. Synthesis of β-ketoesters:
i: N_2CHCO_2Et, $SnCl_2$ cat., CH_2Cl_2, 0 °C, 3 h. ii: H_3CCO_2R'/
LDA, THF, -78 °C, 2 h, then **14** or **19** THF, -78 °C, 12 h.

Again, the conversion of the β-ketoester **15** into the α,β-unsaturated *N*-boc aminoesters **22** and **23** bearing an additional aryl or alkynyl substituent in a *cis*-position with respect to the ester group was achieved by Pd catalysed Stille[17] or Sonogashira[18] cross-coupling reactions, respectively. As pointed out in the aziridine series a one pot procedure gave the best results: Hence the enoltriflates (enol trifluoromethanesulfonates)[20, 28] **21** were generated *in situ* and the subsequnent the cross-coupling reactions in presence of the Pd(0) catalyst, zinc chloride, triphenylarsane[21] and the piperonyl[22] or ethynyl stannane[23], respectively, gave the desired aminoesters **22** in 64% and **23** in 44% yield over two steps. It should be pointed out to keep the reaction time as short as possible generating alkyne **23** because of some alkyne dimerisation under the reaction conditions leading to decreased yields.

The undoubted proofs of the *E*-configurations of the double bonds via NOE analyses failed in the case of the aminoesters **22** and **23**, but succeeded after reduction to the corresponding allylalcohols **24** and **25**, respectively. The appropriate reduction of the esters was carried out with DIBALH[14] in Et_2O at low temperatures to avoid any hydrogenation of the double bonds as known for several *N*-boc allylamines.[29] However, the yields varied between 60% (**24**) and 63% (**25**) despite of several variations of the reaction conditions. The use of Red-Al® or $LiAlH_4$ did not increase the yields of the desired alcohols.



Scheme 4. Cross-coupling reactions:

i: *i*Pr_2NH, THF, -78 °C, 15 min, then Tf_2O, THF, -78 °C, 2 h. ii: $Pd_2(dba_3)(CHCl_3)$ cat., Ph_3As, $ZnCl_2$, *N*-methylpyrrolidone, (3,4-methylenedioxyphenyl)-$SnBu_3$, Et_2O, -50→20°C, 3 d. iii: $Pd_2(dba_3)(CHCl_3)$ cat., Ph_3As, NMP, $TMSC{\equiv}CSnBu_3$, $ZnCl_2$, Et_2O, -50→20°C, 7 d. iv: DIBALH, Et_2O, -20→20°C, 3 h. v: 1. F_3CCO_2H, CH_2Cl_2, 0→20°C, 8 h; 2. TBSCl, Et_3N, CH_2Cl_2, 20 °C, 12 h. vi: $NaBH_4$, EtOH, 0→20°C, 12 h.

The formation of an acyclic *N*-boc allylamine starting from aminoester **18** had been abandoned because of the disappointing yields on synthesising the β-ketoester **19**. On the other hand the successful generation of the allylamines **22** and **23** allowed to achieve an appropriate structure by protective group conversion. Thus the aminoester **22** was treated with TFA (trifluoro acetic acid)[30] to remove boc and acetonide group, the OH function of the crude product was protected as a TBS ether (*t*butyldimethylsilyl ether)[31] to give aminoester **27** in 66% yield. Though the acidolysis was carried out at low temperatures additional trifluoroacetamide **26** was isolated in 32% as a side product, any prolongation of the reaction time increased the yield of the amide. On focusing the synthesis on the deprotected aminoester **27**, the trifluoroacetamide **26** could be reduced with $NaBH_4$ in EtOH[32] to give the desired **27** in about 53% yield (overall yield of **27**: 83% over both reactions). In conclusion, the deprotected amine should serve as an anchoring group for further synthetically useful substituents.[33]

DISCUSSION

The usefulness of α,β-difunctionalised aminoacid esters originating from *L*-(-)-serine to generate the chain elongated β-ketoesters via a Claisen ester condensation depended strongly from the substitution pattern of the starting material, the heterocyclic reactants were recommended: Employing the heterocyclic α-amino-esters **1** and **13** the corresponding β-ketoesters **6** and **15** were synthesised in 70 to 80% yield, respectively.[33] The small 3- and 5-membered rings of **1** and **15** efficiently suppressed the achievement of conformations favouring undesired β-eliminations. In contrast, the reaction with the acyclic ester **18** gave only disappointing yields of **19**. Obviously, the competing β-elimination to **20** was a rather facile process reacting the open chain material: Presumably the suitable arrangement of α-H and β-O-function were easily achieved to generate the double bond under the strongly basic conditions.

The generation of defined trisubstituted olefinic units has been described by L. Weiler:[19] β-Ketoesters were deprotonated to give stereoselectively the *E*- or *Z*-enolates depending strongly from the base involved; an O-acylation with phosphorous acid chlorides gave the corresponding *E*- or *Z*-enol phosphates, respectively. A final metal mediated reaction with alkyl cuprates allowed the exchange of the phosphate against an alkyl substituent with retention of the double bond configuration to form the desired trisubstituted olefins. In contrast, the configuration of the newly formed double bond was found to be *E* in all isolated aminoesters *E*-**4**, **9**, **22** and **23**, no side products bearing *Z*-olefins could be detected. The configuration determining step was presumed to as the enolisation of the β-ketoesters resulting an arrangement of the ester *syn* with respect to the small oxygen and *anti* to the bulky amino substituent in the nascent double bond. Independently from the base involved the *E*-enoltriflates were formed exclusively as the intermediates **8** and **17**, the *E*-configuration was completely transferred into the aminoesters *E*-**4**, **9**, **22** and **23**. Summarising these results, the three step sequence was recommended to convert the aminoesters **1** and **13** selectively into the desired *E*-allylamino compounds *E*-**4**, **9**, **22** and **23**.

CONCLUSION

A short three step sequence to generate optically active *N*-allylamino compounds with defined configurated trisubstituted olefinic units was developed. A Claisen ester condensation served as the first key step to carry out the two-carbon chain elongation. Careful monitoring of the reaction conditions was found to be crucial to achieve high yields of the corresponding β-ketoesters and to suppress any competing reactions. The β-ketoesters were subjected to a one pot procedure of an initial enol trifluoromethanesulfonate formation and a consecutive palladium(0) catalysed cross-coupling reaction. A piperonyl and an ethynyl substituent, respectively, were introduced, pointing out, that metal-mediated cross-couplings succeeded in presence of potential

labile nitrogen functions as the aziridine and the carbamate. The resulting double bonds were found to be exclusively *E*, no *Z*-olefins as detected in the initially described Horner sequence were isolated. The configurations of the double bonds were proved via NOE analyses. Further reactions allowed the chemoselective transformations of the allylamine termini. The DIBALH reduction of the ester groups led to the corresponding allylalcohols and the acid mediated cleavage of the nitrogen protective group generated the amines. Especially, the failing of the sequence starting from the acyclic α-aminoester **18** because of the dissatisfying formation of the corresponding β-ketoester **19** could be compensated by the successful synthesis of the deprotected aminoester **27**; a final boc protection would have formed the corresponding allylcarbamate.

The so formed *N*-allylamino compounds with a defined substitution pattern represent versatile building blocks in total syntheses of natural products. The generation of optically active quarternary centres seems to be a practicable scheme: Michael-type reactions with the unsaturated esters *E*-**4**, **9**, **22** and **23** or Claisen-type rearrangements with the allylalcohols *E*-**5**, **10**, **24** and **25** might serve as key steps. In this regard further investigations are in progress.

EXPERIMENTAL SECTION

General Remarks: ^{1}H NMR (250 MHz),^{13}C NMR (63 MHz) spectra and NOE experiments were recorded on Bruker AC 250 spectrometer. $CDCl_3$ was used as the solvent, tetramethylsilane was used as internal standard, all spectra were measured at room temperature. Multiplets in ^{13}C-NMR spectra were determined by DEPT technique. Illustration of the NOE analysis: irradiation H-X ⇒ amplification at H-Y [%]. IR spectra were obtained from a Perkin Elmer 257 or 580B spectrophotometer as a film in KBr cells or on KBr plates. 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, (70 eV, EI, temperature as specified). High resolution mass spectra (HRMS, 80 eV, temperature as specified for the MS) were recorded with the same instruments using computer assisted methods to compare characteristic fragments with the corresponding PFK peaks. Elemental analysis were performed on a Perkin Elmer 240 Elemental Analyser. Column chromatography was carried out with Merck silica gel 0.063 - 0.2mnm, 70 - 230 mesh A. Process of reaction were monitored by thin layer chromatography (TLC) performed on aluminium sheets precoated with silica gel 60 (thickness 0.25 mm). All solvents were dried before use following standard procedures.

Reagents

3,4-Methylenedioxyphenyl tributylstannane (piperonyl tributylstannane): Under argon, 4-bromo-1,2-methylenedioxybenzene (piperonyl bromide, 10 g, 49.8 mmol) in THF (100 mL) was treated with *n*BuLi (34.2 mL, 54.8 mmol, 1.6 M in *n*hexane) at -78 °C. After 1 h of stirring at that temperature chlorotributylstannane

(22.3 mL, 74.7 mmol) was added. The mixture was stirred at -78 °C for a further 2 h, then, saturated aqueous NH_4Cl (100 mL) was added. The aqueous layer was extracted with Et_2O (3x 150 mL), the combined organic phases were dried ($MgSO_4$). After removal of the solvents the crude oil was purified by high vacuum distillation (bp: 120–140 °C / 0.02 mbar) to give the piperonylstannane (16.8 g, 40.9 mmol, 82%) as a clear oil. ^1H NMR δ = 0.92 (t, J = 7.0 Hz, 9 H; Bu–CH_3), 1.06, 1.40, 1.56 (3x m, 18 H; Bu–CH_2), 5.96 (s, 2 H; OCH_2O), 6.86–7.08 (m, 3 H; Ar–CH). ^{13}C NMR: δ = 9.7 (3 C; Bu–CH_2), 13.7 (3 C; Bu–CH_3), 27.4, 29.0 (6 C; Bu–CH_2), 100.2 (OCH_2O), 108.8, 115.5, 129.6 (Ar–CH), 133.9, 147.4, 147.6 (Ar–C).

Tributyl-(2-trimethylsilylethynyl)-stannane: Reaction with trimethylsilylethyne (1.64 g, 16.7 mmol) using conditions as described for piperonyl tributylstannane. Purification by Kugelrohr distillation (60–70 °C / 0.05 mbar) to give a clear oil of ethynylstannane (6.3 g, 16.3 mmol, 98%). ^1H NMR: δ = 0.22 (s, 9 H; Si–CH_3), 0.80–1.08, 1.36, 1.60 (3x m, 27 H; Bu–CH_2, Bu–CH_3). ^{13}C NMR: δ = 0.2 (3 C; Si–CH_3), 8.7, 11.1 (6 C; Bu–CH_2), 13.6 (3 C; Bu–CH_3), 14.5 (3 C; Bu–CH_2), 113.1, 118.8 (C≡C).

Standard procedures

Standard procedure I: *DIBALH reduction*: Under argon, the α,β-unsaturated ester (10 mmol) in dry Et_2O (20 mL) was treated with DIBALH (18.3 mL, 22 mmol, 1.2 M solution in toluene) at -20 °C. The mixture was stirred for 3 h, while the temperature reached 20 °C. *Acidic work-up*: The reaction was quenched by addition of MeOH (8 mL). Saturated aqueous. NH_4Cl and aqueous $KHSO_4$ (1 M) were added until the Al_2O_3 precipitate dissolved (pH 2 - 3). The aqueous layer was extracted with Et_2O (4x 65 mL) and the combined organic phases were dried (Na_2SO_4). The solvent was removed and the crude material was purified by column chromatography. *Neutral work-up*: MeOH (0.9 mL), H_2O (1.4 mL) and solid potassium sodium tartrate (~2.5 g) were added and the mixture was stirred, until the aluminium salts precipitated (~12 h). The liquid phase was decanted and the remaining solid material was extracted by stirring with Et_2O (4x 150 mL). The organic layers were dried ($MgSO_4$), the solvent was removed and the crude allylalcohol was purified by column chromatography.

Standard procedure II: *Claisen condensation*: Under argon, diisopropylamine (7.1 mL, 50 mmol) in dry THF (100 mL) was treated with *n*BuLi (27 mL, 43.2 mmol, 1.6 M in hexane) at -78°C. After 1 h of stirring at 0 °C the LDA solution was cooled again to -78 °C. EtOAc (4 mL, 40 mmol) was slowly injected by means of a syringe, the stirring of the mixture was carefully monitored to avoid any spattering - any warming up of small volumes of the reaction mixture would have led to the formation of acetoacetate **7** or **17** decreasing the yield of the desired β-ketoester! Any vigorous stirring should be avoided. After 1 h of deprotonation at - 78°C the reactant aminoester (20 mmol) in THF (40.5 mL) was added slowly maintaining (carefully!) the temperature and the mixture was stirred overnight at -78°C. Then, *i*PrOH (5 mL) was added. After quenching with saturated aqueous NH_4Cl (140 mL) the aqueous layer was extracted with EtOAc (3x 140 mL), the combined or-

ganic phases were dried ($MgSO_4$), the solvent was evaporated and the crude β-ketoester was purified by column chromatography on silica gel to separate from any acetoacetate **7** or **17** or from the elimination product **20**.

Standard procedure III: One pot reaction of *enol-triflate generation* and *Pd-catalysed cross-coupling*: Under argon, the β-ketoester (10 mmol) was dissolved in dry THF (50.6 mL) and cooled to -78 °C. Dry diisopropylamine (3.3 mL, 25 mmol) was injected, after 15 min of stirring trifluoromethanesulfonic acid anhydride (7g, 25 mmol) was added dropwise. The mixture was stirred at -78 °C for 2 h, until the reactant disappeared (tlc monitoring). After raising the temperature to about -50 °C, *N*-methylpyrrolidone (30.3 mL), $Pd_2(dba_3)(CHCl_3)$ (0.21 g, 2 mol%) and Ph_3As (0.25 g, 8 mol%) were added subsequently. Then, the reaction flask was evacuated trice (-50 °C) regenerating each time the argon atmosphere. Finally, the stannane (10 to 20 mmol), dry $ZnCl_2$ (1.68 g, 12 mmol) and dry Et_2O (6.1 mL) were added subsequently and the mixture was stirred for 3 d to 7 d while the temperature reached 20 °C. Work-up started by dilution with Et_2O (56 mL) and cleavage with H_2O (70 mL). The aqueous layer was extracted with Et_2O (4x 56 mL), The organic layers were dried ($MgSO_4$) and the solvent was removed. The crude α,β-unsaturated ester was purified by column chromatography.

Compounds

(2*S*)-1-(3,4-Methylenedioxyphenyl)-2,3-(*N*-triphenylmethylepimino)-1-propanol (3): *Swern oxidation*: Under argon, to a solution of oxalyl chloride (1.57 mL, 18 mmol) in dry CH_2Cl_2 (36 mL) was added dry DMSO (1.34 mL, 18.8 mmol) at -65 °C, with stirring. After 30 min *N*-tritylaziridinecarbinol **2** (2.7 g, 8.56 mmol) in dry CH_2Cl_2 (17 mL) was added dropwise. After a further 1.5 h of stirring at -65 °C, Et_3N (10.5 mL, 75.3 mmol) was added and the mixture was stirred at -65 °C for 20 min and at 20 °C for another 2 h. The white precipitate of Et_3N/HCl was formed. Then, the reaction was quenched with H_2O (60 mL); the aqueous layer was extracted with CH_2Cl_2 (3x 50 mL) and the combined organic layers were dried ($MgSO_4$). After removal of the solvent, the crude aldehyde was used without any further purification. *Grignard reaction*: Under argon, piperonyl bromide (1.55 mL, 12.84 mmol) in dry THF (51 mL) was treated with *n*BuLi (8 mL, 12.8 mmol, 1.6 M in *n*hexane) at -78 °C. After 1.5 h of stirring at that temperature, the crude aldehyde (~ 8.56 mmol) in THF (15 mL) was added. The mixture was stirred overnight while the temperature reached 20 °C. The reaction was quenched with H_2O (80 mL) and the organic layer was extracted wit Et_2O (3x 60 mL). After drying ($MgSO_4$), the solvent was removed and the crude material was purified by chromatography on silica gel (hexane/EtOAc 10 : 1) to give **3** (2.4 g, 5.51 mmol, 64%, colourless oil) as a mixture of diastereomers, which had not been separated. IR: $\tilde{\nu}$ = 3563 (m), 3447 (m, br), 3057 (s), 3020 (s), 2982 (s), 2891 (s), 1737 (s), 1595 (s), 1488 (s), 1447 (s) cm^{-1}. ^1H NMR: δ = 1.08 (d, *J* = 6.3 Hz, 1 H; 3–H^A), 1.54 (m, 1 H; 2–H), 1.81 (d, *J*

= 3.5 Hz, 1 H; 3–H^B), 2.64 (s, br, 1 H; OH), 4.43 (d, J = 5.5 Hz, 1 H; 1–H), 5.80 (s, 2 H; OCH_2O), 6.54–6.76 (m, 3 H; Ar–CH), 7.04–7.53 (m, 15 H, Ph_3C–CH). ^{13}C NMR: δ = 25.4 (C–3), 27.9 (C–2), 73.7 ($NCPh_3$), 75.0 (C–1), 100.9 (OCH_2O), 106.5, 107.9, 119.2 (Ar–CH), 126.7 – 129.5 (15 C; Ph_3C–CH), 136.1 (Ar–C), 144.1 (3 C; Ph_3C–C), 146.8, 147.5 (Ar–C). MS (180 °C): m/z = 435 (0.6, M^+), 244 (8.0), 243 (100), 228 (4.5), 166 (7.9), 165 (49.4), 151 (11.1), 93 (8.5), 91 (6.9), 65 (4.4). HRMS (M^+: $C_{29}H_{25}NO_3$): calc.: 435.1834, found: 435.1835.

(4*R*)-*Z*-3-(3,4-Methylenedioxyphenyl)-4,5-(*N*-triphenylmethylepimino)-2-pentenoicacid ethylester (*Z*-4) and (4*R*)-*E*-3-(3,4-methylenedioxyphenyl)-4,5-(*N*-triphenylmethylepimino)-2-pentenoicacid ethylester (*E*-4): *Swern oxidation*: The Swern oxidation was carried out with carbinol **3** (1.43 g, 3.28 mmol) to give the corresponding ketone as described for the synthesis of carbinol **3**. *Horner olefination*: Under argon, triethyl phosphonoacetate (2.07 mL, 10.5 mmol) in dry THF (42 mL) was deprotonated with NaH (0.3 g, 10.5 mmol, 80% in oil) at 0 °C. The reaction was completed by stirring for 2 h at 20 °C. Then, a freshly prepared solution of the crude ketone (~3.28 mmol) in THF (6.6 mL) was injected and the mixture was stirred for 2 d at 20 °C. The reaction was quenched with H_2O (100 mL), extracted with Et_2O (3x 70 mL) and the organic layers were dried ($MgSO_4$). After removal of the solvent the crude oil was purified by chromatography on silica gel (hexane/EtOAc 12 : 1) to give *Z*-**4** (0.28 g, 0.56 mmol, 17%) and *E*-**4** (0.68 g, 1.35 mmol, 41%) as clear oils. Data for the intermediate 3,4-methylenedioxyphenyl-(1*S*-*N*-triphenylmethylaziridinyl)-ketone ^1H NMR: δ = 1.57 (m, 1 H; 3–H^A), 2.41 (m, 1 H; 3–H^B), 2.62 (m, 1 H; 1–H), 6.01 (s, 2 H; OCH_2O), 6.63–6.88 (m, 3 H; Ar–CH), 7.08–7.62 (m, 15 H; Ph_3C–CH). Spectral data for *Z*-**4**: $[\alpha]_D^{20}$ = –24.8° (c = 0.23; $CHCl_3$). IR: $\tilde{\nu}$ = 3057 (s), 2981 (s), 2899 (s), 1715 (s), 1626 (s), 1603 (s), 1488 (s), 1447 (s), 1398 (m), 1344 (m), 633 (m) cm^{-1}. ^1H NMR: δ = 1.08 (t, J = 7.5 Hz, 3 H; Et–CH_3), 1.21 (d, J = 6.0 Hz, 1 H; 5–H^A), 1.80 (d, J = 3.0 Hz, 1 H; 5–H^B), 3.53 (m, 1 H; 4–H), 3.92 (q, J = 7.5 Hz, 2 H; Et–CH_2), 5.89 (s, 2 H; OCH_2O), 5.95 (s, 1 H; 2–H), 6.73–7.49 (m, 18 H; Ar–CH, Ph_3C–CH). NOE analysis: 5–H^A ⇒ 5–H^B (29.8), 4–H (11), Ar–H^6 (0.6), Ar–H^2 (1); 5–H^B ⇒ 5–H^A (31.4), 4–H (1.9), Ar–H^6 (4), Ar–H^2 (6); 4–H ⇒ 5–H^A (6.3), 5–H^B (1.2), 2–H (2.1), Ar–H^2 (0.8); 2–H ⇒ 4–H (0.9), Ar–H^6 (7.2), Ar–H^2 (6.1); Ar–H^6 ⇒ 5–H^B (1.4), 4–H (0.5), 2–H (10.2), Ar–H^2 (2); Ar–H^2 ⇒ 5–H^A (0.5) 5–H^B (1.9), 4–H (0.7), 2–H (7.2), Ar–H^6 (3). ^{13}C NMR: δ = 14.2 (Et–CH_3), 28.6 (C–5), 31.1 (C–4), 59.8 (Et–CH_2), 75.0 ($NCPh_3$), 101.1 (OCH_2O), 107.9, 108.6 (Ar–CH), 121.7, 123.0 (C–2, Ar–CH), 126.6 – 129.6 (15 C; Ph_3C–CH), 133.3 (Ar–C), 144.3 (3 C; Ph_3C –C), 147.3, 147.6 (Ar–C), 156.8 (C–3), 165.8 (C=O). MS (120 °C): m/z = 503 (0.1, M^+), 260 (10.2), 259 (6.5), 244 (42.3), 243 (100), 241 (5.6), 228 (6.6), 216 (10.6), 166 (5.4), 165 (44.3). HRMS: (fragment: $C_{14}H_{14}NO_4$) calc.: 260.0923, found: 260.0922.

Spectral data for *E*-**4**: $[\alpha]_D^{20}$ = –137.6° (c = 0.81; $CHCl_3$). IR: $\tilde{\nu}$ = 3055 (w), 2978 (m), 2897 (w), 1720 (s), 1635 (m), 1489 (s), 1240 (s), 1169 (s), 1037 (s), 707 (s) cm^{-1}. ^1H NMR: δ = 1.21 (t, J = 7.0 Hz, 3 H; Et–CH_3), 1.50 (d, J = 6.0 Hz, 1 H; 5–H^A), 1.92 (m, 2 H; 4–H, 5–H^B), 4.08 (q, J = 7.0 Hz, 2 H; Et–CH_2), 5.96 (s, 2 H;

OCH_2O), 6.36 (s, 1 H; 2–H), 6.61–6.84 (m, 3 H; Ar–CH), 7.15–7.69 (m, 15 H; Ph_3C–CH). NOE analysis: 5–H^A ⇒ 5–H_B (30.6), 4–H (13.7), 2–H (3); 5–H^B ⇒ 5–H^A (33.7), 4–H (22), 2–H (9.5), Ar–H^6 and Ar–H^2 (6); 4–H ⇒ 5–H^A (5.1), 5–H^B (11), 2–H (8), Ar–H^2 and Ar–H^6(11.7); 2–H ⇒ 5–H^A (1.3), 5–H^B (4.1), 4–H (5.2), Ar–H^2 (0.7); Ar–H^6 ⇒ 5–H^B (1), 4–H (3.1), 2–H (0.5); Ar–H^2 ⇒ 5–H^B (1.2), 4–H (3.4). ^{13}C NMR: δ = 14.1 (Et–CH_3), 32.9 (C–5), 37.4 (C–4), 59.9 (Et–CH_2), 75.2 ($NCPh_3$), 101.0 (Ar–CH_2), 107.9, 108.5 (Ar–CH), 116.6, 121.3 (C–2, Ar–CH), 126.9–129.5 (15 C; Ph_3C–CH), 132.2 (Ar–C), 144.0 (3 C; Ph_3C–C), 147.1, 147.4 (Ar–C), 157.4 (C–3), 166.2 (C=O). MS (300 °C): m/z = 503 (1.2, M^+), 306 (4.7), 377 (4.1), 362 (4.7), 261 (20.9), 260 (100), 259 (96.8), 258 (9.2), 257 (28.3), 256 (15.9). HRMS: (M^+: $C_{33}H_{29}NO_4$) calc.: 503.2097, found: 503.2097.

(4*R*)-*E*-3-(3,4-Methylenedioxyphenyl)-4,5-(*N*-triphenylmethylepimino)-2-pentenoicacid ethylester (*E*-4): Reaction with β-ketoester **6**/Et (0.14 g, 0.35 mmol) and piperonylstannane (0.17 g, 0.42 mmol) following the standard procedure III. Reaction time: 4 d. Chromatography: hexane/EtOAc (20 : 1), yield: allylamine *E*-**4** (40 mg, 0.08 mmol, 23%). For the spectral data of *E*-**4** v. s..

(4*R*)-*E*-3-(3,4-Methylenedioxyphenyl)-4,5-(*N*-triphenylmethylepimino)-2-pentenoicacid isopropylester (*E*-4/*i*Pr): Reaction with β-ketoester **6**/*i*Pr (1.81 g, 4.37 mmol) and piperonylstannane (2.7 g, 6.55 mmol) following the standard procedure III. Reaction time: 6 d. Chromatography: hexane/EtOAc (20 : 1), yield: allylamine *E*-**4**/*i*Pr (0.93 g, 1.8 mmol, 41 %). $[\alpha]_D^{20}$ = −129.9° (c = 1.47; $CHCl_3$). IR: $\tilde{\nu}$ = 3056 (w), 3019 (w), 2978 (m), 1717 (s), 1636 (w), 1489 (s), 1445 (s), 1240 (s), 1107 (s), 1038 (s), 708 (s) cm^{-1}. ^{1}H NMR: δ = 1.20 (d, *J* = 6.3 Hz, 6 H; *i*Pr–CH_3), 1.50 (d, *J* = 6.3 Hz, 1 H; 5–H^A), 1.91 (m, 2 H; 4–H, 5–H^B), 4.97 (m, 1 H; *i*Pr–CH), 5.93 (s, 2 H; OCH_2O), 6.32 (s, 1 H; 2–H), 6.61–6.80 (m, 3 H; Ar–CH), 7.13–7.60 (m, 15 H; Ph_3C–CH). ^{13}C NMR: δ = 21.7 (2 C; *i*Pr–CH_3), 32.6 (C–5), 37.5 (C–4), 67.2 (*i*Pr–CH), 75.2 ($NCPh_3$), 101.0 (OCH_2O), 107.8, 108.5 (Ar–CH), 117.3 (C–2), 121.3 (Ar–CH), 126.8–129.5 (15 C; Ph_3C–CH), 132.3 (Ar–C), 144.0 (3 C; Ph_3C–C), 147.0, 147.2 (Ar–C), 156.6 (C–3), 165.8 (C=O). MS (180 °C): m/z = 517 (0.3, M^+), 274 (3.1), 273 (3.1), 245 (2.2), 244 (20.8), 243 (100), 232 (3.4), 165 (11.4). HRMS: (M^+: $C_{34}H_{31}NO_4$) calc.: 517.2253, found: 517.2256.

(4*R*)-*Z*-3-(3,4-Methylenedioxyphenyl)-4,5-(*N*-triphenylmethylepimino)-2-penten-1-ol (*Z*-5): Reaction with α,β-unsaturated ester *Z*-**4** (0.29 g, 0.57 mmol) following the standard procedure I, neutral work-up. Reaction time: 2 h. Chromatography: hexane/EtOAc (7 : 1), yield: allylalcohol *Z*-**5** (0.18 g, 0.39 mmol, 68 %). $[\alpha]_D^{20}$ = −20.8° (c = 0.12; $CHCl_3$). IR: $\tilde{\nu}$ = 3389 (m, br), 3018 (m), 2888 (m), 1595 (m), 1486 (s), 1447 (s), 1236 (s), 1040 (s), 757 (s), 708 (s) cm^{-1}. ^{1}H NMR: δ = 1.35 (d, *J* = 6.3 Hz, 1 H; 5–H^A), 1.95 (m, 2 H; 5–H^B, OH), 2.14 (m, 1 H; 4–H), 4.16 (m ,2 H; 1–H), 5.95 (m, 3 H; 2–H, OCH_2O), 6.72–7.05 (m, 3 H; Ar–CH), 7.16–7.58 (m, 15 H; Ph_3C–CH). ^{13}C NMR: δ = 27.2 (C–5), 32.2 (C–4), 58.7 (C–1), 75.1 ($NCPh_3$), 100.8

(OCH_2O), 107.8, 108.4, 121.2 (Ar–CH), 126.3–129.4 (15 C; Ph_3C–CH), 132.4 (C–2), 135.1, 140.2 (C–3, Ar–C), 144.0 (3 C; Ph_3C–C), 146.6, 147.1 (Ar–C). MS (150 °C): m/z = 461 (0.1, M^+), 431 (0.2), 384 (0.2), 244 (23.1), 243 (100), 218 (6.0), 189 (7.1), 165 (21.8), 86 (13.8), 84 (20.8). HRMS: (M^+: $C_{31}H_{27}NO_3$) calc.: 461.1991, found: 461.1977. (fragment $C_{30}H_{25}NO_2$) calc.: 431.1985 found: 431.1977.

(4*R*)-*E*-3-(3,4-Methylenedioxyphenyl)-4,5-(*N*-triphenylmethylepimino)-2-penten-1-ol (*E*-5): Reaction with α,β-unsaturated ester **6**/iPr (0.93 g, 1.8 mmol) following the standard procedure I, acidic work-up. Reaction time: 3 h. Chromatography: hexane/EtOAc (4 : 1), yield: allylalcohol *E*-**5** (0.59 g, 1.28 mmol, 71 %). $[\alpha]_D^{20}$ = −136.9° (c = 0.31; $CHCl_3$). IR: $\tilde{\nu}$ = 3390 (w, br), 3055 (w), 2883 (w), 1595 (w), 1488 (s), 1236 (s), 1038 (s), 1012 (m), 708 (s), 633 (m) cm^{-1}. ^1H NMR: δ = 1.34 (d, *J* = 6.3 Hz, 1 H; 5–H^A), 1.72 (d, *J* = 2.0 Hz, 1 H; 5–H^B), 1.84 (m, 1 H; 4–H), 1.96 (s, br, 1 H; OH), 4.16 (d, *J*= 7.0 Hz , 2 H; 1–H), 5.92 (s, 2 H; OCH_2O), 6.05 (t, *J* = 7.0 Hz, 1 H; 2–H), 6.56–6.82 (m, 3 H; Ar–CH), 7.12–7.60 (m, 15 H; Ph_3C–CH). ^{13}C NMR: δ = 29.8 (C–5), 36.9 (C–4), 59.9 (C–1), 74.9 ($NCPh_3$), 100.8 (OCH_2O), 107.8, 108.9, 121.9 (Ar–CH), 126.6–129.5 (16 C; C–2, Ph_3C–CH), 131.9 (Ar–C), 141.7 (C–3), 144.2 (3 C; Ph_3C–C), 146.6, 147.2 (Ar–C). MS (180 °C): m/z = 461 (0.1, M^+), 443 (0.2), 384 (0.2), 244 (21.5), 243 (100), 218 (5.8), 200 (5.9), 188 (5.5), 165 (16.4). HRMS: (fragment $C_{31}H_{25}NO_2$) calc.: 443.1885, found: 443.1886. (fragment $C_{25}H_{22}NO_3$) calc.: 384.1600, found: 384.1599.

(4*S*)-3-Oxo-4,5-(*N*-triphenylmethylepimino)-pentanoicacid ethylester (6/Et): Reaction with aminoester **1** (9.8 g, 28.6 mmol) following the standard procedure II. Chromatography: hexane/EtOAc (10 : 1), yield: β-ketoester **6**/Et (8.9 g, 22.3 mmol, 78%). $[\alpha]_D^{20}$ = −51.8° (c = 0.67; $CHCl_3$). IR: $\tilde{\nu}$ = 3319 (m), 3057 (m), 2984 (m), 1960 (w), 1743 (s), 1699 (s), 1575 (s), 1033 (s), 902 (m), 708 (s), 625 (m) cm^{-1}. ^1H NMR: δ = 1.26 (t, *J* = 7.0 Hz, 3 H; Et–CH_3), 1.50 (d, *J* = 6.3 Hz, 1 H; 5–H^A), 2.11 (m, 1 H; 4–H), 2.28 (m, 1 H; 5–H^B), 3.68 (s, 2 H; 2–H), 4.16 (q, *J* = 7.0 Hz, 2 H; Et–CH_2), 7.14–7.56 (m, 15 H, Ph_3C–CH). ^{13}C NMR: δ = 14.1 (Et–CH_3), 29.1 (C–5), 39.1 (C–4), 44.3 (C–2), 61.4 (Et–CH_2), 74.5 ($NCPh_3$), 126.9–129.3 (15 C; Ph_3C–CH), 143.2 (3 C; Ph_3C–C), 167.1 (C=O), 201.5 (C=O). MS (120 °C): m/z = 399 (0.4, M^+), 322 (1.9), 245 (2.4), 244 (23.5), 243 (100), 242 (2.2), 241 (3.3), 228 (2.5), 166 (2.9), 165 (18.7). HRMS: (M^+: $C_{26}H_{25}NO_3$) calc.: 399.1834, found: 399.1829.

(4*S*)-3-Oxo-4,5-(*N*-triphenylmethylepimino)-pentanoicacid isopropylester (6/*i*Pr): Reaction with aminoester **1** (16.2 g, 47.2 mmol) and *i*PrOAc (7.23 g, 8.29 mL, 70.8 mmol) following the standard procedure II. Chromatography: hexane/EtOAc (12 : 1), yield: β-ketoester **6**/*i*Pr (13.6 g, 32.9 mmol, 70%). $[\alpha]_D^{20}$ = −83.2° (c = 2.33; $CHCl_3$). IR: $\tilde{\nu}$ = 2982 (m), 1740 (s), 1710 (s), 1490 (m), 1448 (m), 1106 (s), 1006 (m), 913 (m), 708 (s) cm^{-1}. ^1H NMR: δ = 1.21 (d, *J* = 6.3 Hz, 6 H; *i*Pr–CH_3), 1.48 (d, *J* = 6.3 Hz, 1 H; 5–H^A), 2.11 (m, 1

H; 4–H), 2.28 (m, 1 H; 5–H^B), 3.68 (s, 2 H; 2–H), 5.05 (m, 1 H; *i*Pr–CH), 7.12–7.56 (m, 15 H, Ph_3C–CH). ^{13}C NMR: δ = 21.6 (2 C; *i*Pr–CH_3), 29.1 (C–5), 39.0 (C–4), 44.7 (C–2), 68.9 (iPr–CH), 74.4 ($NCPh_3$), 127.0–129.1 (15 C; Ph_3C–CH), 143.2 (3 C; Ph_3C–C), 166.6 (C=O), 201.4 (C=O). MS (120 °C): m/z = 413 (0.5, M^+), 370 (2.8), 336 (18.8), 294 (25.6), 271 (7.2), 244 (53.0), 243 (100), 241 (9.3), 228 (7.5), 165 (44.8). HRMS: (M^+: $C_{27}H_{27}NO_3$) calc.: 413.1991. found: 413.1983.

(1'*R*)-*E*-5-Trimethylsilyl-3-(*N*-triphenylmethylaziridinyl)-2-penten-4-ynoicacid isopropylester (9): Reaction with β-ketoester **6/*i*Pr** (1.99 g, 4.81 mmol) and trimethylsilylethynylstannane (3.73 g, 9.6 mmol) following the standard procedure III. Reaction time: 7 d. Chromatography: hexane/EtOAc (12 : 1), yield: allylamine **9** (1.03 g, 2.1 mmol, 44%). $[\alpha]_D^{20}$ = −47.2° (c = 0.33; $CHCl_3$). IR: $\tilde{\nu}$ = 3058 (w), 2930 (s), 2148 (w), 1723 (s), 1611 (m), 1448 (m), 1250 (s), 1109 (s), 844 (s), 708 (s) cm^{-1}. ^1H NMR: δ = 0.31 (s, 9 H; Si–CH_3), 1.37 (d, *J* = 6.3 Hz, 6 H; *i*Pr–CH_3), 1.64 (m, 1 H; 3'–H^A), 1.86 (m, 1 H; 1'–H), 2.08 (m, 1 H; 3'–H^B), 5.12 (m, 1 H; *i*Pr–CH), 6.17 (s, 1 H; 2–H), 7.16–7.56 (m, 15 H; Ph_3C–CH). ^{13}C NMR: δ = −0.3 (3 C; Si–CH_3), 17.5 (C–3'), 21.9 (C–1'), 36.8 (2 C; *i*Pr–CH_3), 67.7 (iPr–CH), 74.7 ($NCPh_3$), 100.1, 108.2 (C≡C), 124.8 (C–2), 126.8–129.4 (15C; Ph_3C–CH), 138.3 (C–3), 144.0 (3 C; Ph_3C–C), 164.3 (C=O). MS (150 °C): m/z = 450 (0.2), 244 (20.2), 243 (100), 241 (6.7), 239 (7.8), 228 (6.7), 215 (5.3), 166 (8.5), 165 (56.5), 43 (4.6).

(1'*R*)-*E*-5-Trimethylsilyl-3-(*N*-triphenylmethylaziridinyl)-2-penten-4-yn-1-ol (10): Reaction with α,β-unsaturated ester **6/*i*Pr** (0.77 g, 1.56 mmol) following the standard procedure I, acidic work-up. Reaction time: 3 h. Chromatography: hexane/EtOAc (6 : 1), yield: allylalcohol **10** (0.31 g, 0.71 mmol, 46%). $[\alpha]_D^{20}$ = −82.5° (c = 0.04; $CHCl_3$). IR: $\tilde{\nu}$ = 3357 (m, br), 3033 (m), 2959 (m), 2145 (m), 1595 (m), 1490 (s), 1448 (s), 1250 (s), 1017 (s), 843 (s), 708 (s) cm^{-1}. ^1H NMR: δ = 0.26 (s, 9 H; Si–CH_3), 1.28 (m, 1 H; 3'–H^A), 1.73 (m, 1 H; 1'–H), 2.01 (m, 1 H; 3'–H^B), 4.42 (m, 2 H; 1–H), 6.12 (m, 1 H; 2–H), 7.10–7.63 (m, 15 H; Ph_3C–CH). ^{13}C NMR: δ = −0.1 (3 C, Si–CH_3), 27.8 (C–3'), 35.4 (C–1'), 61.3 (C–1), 74.4 ($NCPh_3$), 100.1, 101.4 (C≡C), 125.5 (C–3), 126.6–129.4 (15 C; Ph_3C–CH), 136.8 (C–2), 144.3 (3 C; Ph_3C–C). MS (200 °C): m/z = 437 (0.2, M^+), 245 (4.0), 244 (26.5), 243 (100), 180 (4.9), 166 (7.6), 165 (36.8), 77 (5.2), 75 (5.3), 73 (15.9). HRMS: (M^+: $C_{29}H_{31}NOSi$) calc.: 437.2175, found: 437.2177.

(4*R*)-*E*-4,5-Epimino-3-(3,4-methylenedioxyphenyl)-2-pentenoicacid ethylester (11) and (4*R*)-*E*-4,5-(*N*-(1,3-dioxo-3-methoxypropyl)-epimido)-3-(3,4-methylenedioxyphenyl)-2-pentenoicacid ethylester (12): *Deprotection*: At -20 °C, the α,β-unsaturated ester ***E*-4/Et** (0.89 g, 1.77 mmol) in $CHCl_3$ (9.7 mL) was treated with MeOH (0.14 mL, 3.54 mmol) and a mixture of formic acid/$CHCl_3$ (2.7 mL, 1 : 1), with stirring. After 6 h at -20 °C no reactant remained (tlc-monitoring) and toluene (12 mL) was added as well as K_2CO_3 until the pH was raised to ≥ 7. The reaction mixture was dried by adding an excess of $MgSO_4$, the salts were filtered off and the solvent was removed to give the crude aziridine **11**, a further purification was achieved by

flash chromatography on a short silicagel column with hexane/EtOAc (1 : 1) to give **11** (0.32 g, 1.23 mmol, 70%) as a pale yellow oil. *Acylation*: At -20 °C, the crude aziridine **11** in dry THF (7.3 mL) was subsequently treated with Et_3N (0.62 mL, 13 mmol) and malonic acid monomethylester chloride (0.31 g, 2.3 mmol) with stirring. After 12 h (the temperature reached 20 °C) the reaction was hydrolysed with H_2O (20 mL). The aqueous layer was extracted with Et_2O (3x 10 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was removed. The crude material was purified by chromatography on silica gel with hexane/EtOAc (2 : 1) to give the malonic acid amide **12** (0.47 g, 1.3 mmol, 74%) as a clear oil.

Spectral data of **11**: ^{1}H NMR: δ = 1.13 (t, *J* = 7.0 Hz, 3 H; Et–CH_3), 1.19 (m, 1 H; NH), 1.60 (d, *J* = 3.0 Hz, 1 H; 5–H^A), 2.00 (d, *J* = 5.5 Hz, 1 H; 5–H^B), 2.69 (m, 1 H; 4–H), 4.04 (q, *J* = 7.0 Hz, 2 H; Et–CH_2), 5.95 (s, 2 H; OCH_2O), 6.09 (s, 1 H; 2–H), 6.57–6.96 (m, 3 H; Ar–CH). ^{13}C NMR: δ = 14.0 (Et–CH_3), 27.0 (C–5), 35.1 (C–4), 59.9 (Et–CH_2), 101.1 (OCH_2O), 108.0, 108.7 (Ar–CH), 118.0, 121.8 (C–2, Ar–CH), 138.2, 147.3, 147.6 (Ar–C), 156.2 (C–3), 165.5 (C=O).

Spectral data of **12**: $[\alpha]_D^{20}$ = –40.0° (c = 0.23; $CHCl_3$). IR: $\tilde{\nu}$ = 3360 (w, br), 2984 (m), 2955 (m), 2903 (m), 1744 (s), 1708 (s), 1490 (s), 1439 (s), 1039 (s), 935 (m) cm^{-1}. ^{1}H NMR: δ = 1.13 (t, *J* = 7.5 Hz, 3 H; Et–CH_3), 2.18 (m, 1 H; 5–H^A), 2.75 (m, 1 H; 5–H^B), 3.30 (m, 1 H; 4–H), 3.50 (s, 2 H; O=CCH_2), 3.74 (s, 3 H; OCH_3), 4.04 (q, *J* = 7.5 Hz, 2 H; Et–CH_2), 5.96 (s, 2 H; OCH_2O), 6.11 (s, 1 H; 2–H), 6.63–6.84 (m, 3 H; Ar–CH). ^{13}C NMR: δ = 13.7 (Et–CH_3), 33.7 (C–5), 40.6 (C–4), 43.6 (O=CCH_2), 52.6 (OCH_3), 60.2 (Et–CH_2), 101.22 (OCH_2O), 108.0, 108.6 (Ar–CH), 118.6 (C–2), 121.6 (Ar–CH), 129.2, 147.3, 147.9 (Ar–C), 151.4 (C–3), 165.4, 167.3, 176.7 (N–CO, 2x C=O). MS (120 °C): m/z = 361 (58.8, M^+), 288 (19.2), 260 (43.4), 244 (33.3), 232 (78.4), 216 (45.9), 214 (35.2), 204 (66.1), 188 (100), 187 (45.8), 101 (31.1), 59 (25.1). HRMS: (M^+: $C_{18}H_{19}NO_7$) calc.: 361.1162, found: 361.1187.

(4*S*)-4N,5O-(*N*-*t*Butyloxycarbonylisopropylidenazoxy)-3-oxopentanoicacid ethylester (15): Under argon, a mixture of $SnCl_2$ (1.35 g, 7.18 mmol) and ethyl diazoacetate (8.2 g, 71.8 mmol) in dry CH_2Cl_2 (130 mL) was treated with aldehyde **14** (13.7 g, 59.8 mmol) in CH_2Cl_2 (50 mL) at 0 °C with stirring. Stirring was continued at 0 °C for about 3 h, until the N_2-evolvement finished. Then, the suspension was filtered (Celite) and the solvent was removed under reduced pressure. The residue was dissolved in Et_2O (250 mL), after extraction with aqueous NaOH (6x 100mL, 0.1 N) the combined aqueous layers were acidified with aqueous $KHSO_4$ (1 M) to pH 3. The aqueous solution was extracted with Et_2O (3x 200 mL) and the combined organic phases were dried ($MgSO_4$). Finally, the solvent was removed to give pure β-ketoester **16** (7.6 g, 24.1 mmol, 40%), no chromatography was necessary. $[\alpha]_D^{20}$ = –56.8° (c = 1.94; $CHCl_3$). IR: $\tilde{\nu}$ = 2982 (s), 2938 (m), 1751 (s), 1712 (s), 1479 (m), 1458 (m), 1367 (s), 1172 (s), 849 (m), 769 (m) cm^{-1}. ^{1}H NMR: δ = 1.28 (t, *J* = 7.0 Hz, 3 H; Et–CH_3), 1.36–1.80 (m, 15 H; ketal–CH_3, *t*Bu–CH_3), 3.55 (m, 2 H; 2–H), 3.96–4.29 (m, 4 H; 5–H, Et–CH_2), 4.40, 4.54 (2x m, 1 H; 4–H). ^{13}C NMR: δ = 14.0 (Et–CH_3), 23.5–26.0 (2 C; ketal–CH_3), 28.1 (3 C; *t*Bu–

CH_3), 45.5 (C–2), 61.3 (Et–CH_2), 65.2 (C–4), 65.4 (C–5), 81.1 (O–CMe_3), 95.2 ($OCMe_2O$), 151.1 (NC=O), 166.7 (C=O), 201.1 (C=O). MS (60 °C): m/z = 315 (1.0, M^+), 300 (2.0), 259 (2.8), 242 (2.7), 200 (31.6), 154 (16.6), 115 (7.8), 100 (60.2), 57 (100), 43 (11.8). HRMS: (M^+: $C_{15}H_{25}NO_6$) calc.: 315.1682, found: 315.1692.

(4*S*)-4N,5O-(*N*-*t*-Butyloxycarbonylisopropylidenazoxy)-3-oxopentanoicacid ethylester (15): Reaction with aminoester **13** (3.66 g, 14.5 mmol) following the standard procedure II. Chromatography: hexane/EtOAc (7 : 1), yield: β-ketoester **15** (3.5 g, 11.1 mmol, 77%). For spectral data v. s.

(4*S*)-5-*t*Butyldimethylsilyloxy-4-(*N*-*t*butyloxycarbonylamido)-3-oxopentanoicacid isopropylester (19): Reaction with aminoester **18** (0.5 g, 1.5 mmol) following the standard procedure. Chromatography: hexane/EtOAc (6 : 1), yield: β-ketoester **19** (0.14 g, 0.35 mmol, 23%). ^{1}H NMR: δ = 0.00 (s, 6 H; Si–CH_3), 0.81 (s, 9 H; *t*Bu), 1.19 (d, *J* = 6.5 Hz, 6 H; *i*Pr–CH_3), 1.39 (s, 9 H; boc–CH_3), 3.50 (s, 2 H; 2–H), 3.73 (dd, *J* = 4.5, 10.5 Hz, 1 H; 5–H^A), 4.00 (dd, *J* = 3.3, 10.5 Hz, 1 H; 5–H^B), 4.34 (m, 1 H; 4–H), 4.98 (m, 1 H; *i*Pr–CH), 5.35 (d, br, *J* = 7 Hz, 1 H; NH). ^{13}C NMR: δ = –5.7 (2 C; Si–CH_3), 18.1 (Si–C), 21.6 (2 C; *i*Pr–CH_3), 25.7 (*t*Bu–CH_3), 28.2 (boc–CH_3), 45.2 (C–2), 61.2 (C–4), 63.0 (C–5), 68.9 (iPr–CH), 79.9 (O–CMe_3), 155.2 (NC=O), 166.2 (C=O), 201.0 (C=O).

(4*R*)-*E*-4N,5O-(*N*-*t*Butyloxycarbonylisopropylidenazoxy)-3-(3,4-methylenedioxyphenyl)-2-pentenoicacid ethylester (22): Reaction with β-ketoester **15** (4.5 g, 14.3 mmol) and piperonylstannane (6 g, 14.3 mmol) following the standard procedure III. Reaction time: 3 d. Chromatography: hexane/EtOAc (6 : 1), yield: allylamine **22** (3.8 g, 9.1 mmol, 64%). $[\alpha]_D^{20}$ = +48.9° (c = 0.33; $CHCl_3$). IR: $\tilde{\nu}$ = 2979 (s), 2935 (s), 1726 (s), 1701 (s), 1653 (m), 1490 (s), 1376 (s), 1365 (s), 856 (m), 770 (m) cm^{-1}. ^{1}H NMR: δ = 1.01 (m, 3 H; Et–CH_3), 1.26–1.67 (m, 15 H; ketal–CH_3, *t*Bu–CH_3), 3.67 (m, 1 H; 5–H^A), 3.91 (m, 3 H; 5–H^B, Et–CH_2), 4.45, 4.55 (2x m, 1 H; 4–H), 5.82 (m, 3 H; 2–H, OCH_2O), 6.49–6.72 (m, 3 H; Ar–CH). ^{13}C NMR: δ = 13.3, 13.7 (Et–CH_3), 22.6 – 26.3 (2 C; ketal–CH_3), 28.1 (*t*Bu–CH_3), 59.5 (Et–CH_2), 63.2, 63.5 (C–4), 66.5 (C–5), 80.0, 80.4 (*t*Bu–C), 94.3, 94.7 ($OCMe_2O$), 100.9 (OCH_2O), 107.8, 108.3, 116.7 (Ar–CH), 121.1 (C–2), 130.8, 147.1, 147.3 (Ar–C), 151.4 (NC=O), 155.8, 156.1 (C–3), 165.3 (C=O). MS (70 °C): m/z = 419 (20.6, M^+), 361 (4.0), 319 (32.2), 305 (23.7), 304 (26.1), 261 (47.3), 216 (18.3), 188 (17.0), 100 (29.8), 57 (100). HRMS: (M^+: $C_{22}H_{29}NO_7$) calc.: 419.1944, found: 419.1945. Analysis: $C_{22}H_{29}NO_7$: calc.: C / H = 9.04, found: C / H = 9.03.

(1'*R*)-*E*-3-(2N,4O-*N*-*t*Butyloxycarbonyl-3,3-dimethyloxazolidinyl)-5-trimethylsilyl-2-penten-4-ynoicacid ethylester (23): Reaction with β-ketoester **15** (3.55 g, 11.2 mmol) and trimethylsilylethynylstannane (3.18 g, 22.4 mmol) following the standard procedure III. Reaction time: 7 d. Chromatography: hexane/EtOAc (10 : 1), yield: allylamine **23** (1.92 g, 4.93 mmol, 44%). $[\alpha]_D^{20}$ = –48.5° (c = 2.00; $CHCl_3$). IR: $\tilde{\nu}$ = 2981 (m), 2098 (w), 1706 (s), 1620 (w), 1375 (s), 1251 (s), 1208 (s), 1173 (s), 1097 (s), 848 (s) cm^{-1}. ^{1}H NMR: δ = 0.52

(s, 9 H; Si–CH_3), 1.60 (t, J = 7.0 Hz, 3 H; Et–CH_3), 1.66–2.04 (m, 15 H; ketal–CH_3, *t*Bu), 4.25–4.58 (m, 4 H; 5'–H, Et–CH_2), 4.67, 4.82 (2x m, 1 H; 1'–H), 6.74 (s, 1 H; 2–H). ^{13}C NMR: δ = –6.7 (3 C; Si–CH_3), 14.1 (Et–CH_3), 24.0, 26.4 (ketal–CH_3), 28.1 (3 C; *t*Bu–CH_3), 60.2 (Et–CH_2), 62.5 (C–1'), 67.5 (C–5'), 80.3 ($OCMe_3$), 94.9 ($OCMe_2O$), 99.6, 108.6 (C≡C), 124.8 (C–2), 143.1 (C–3), 151.4 (NC=O), 164.42 (C=O). MS (60 °C): m/z = 395 (2.1, M^+), 332 (36.7), 281 (17.4), 280 (44.0), 208 (9.8), 165 (15.1), 100 (15.7), 73 (16.9), 57 (100), 41 (14.0).

(4*R*)-*E*-4N,5O-(*N*-*t*Butyloxycarbonylisopropylidenazoxy)-3-(3,4-methylenedioxyphenyl)-2-penten-1-ol (24): Reaction with α,β-unsaturated ester **22** (5.2 g, 12.4 mmol) following the standard procedure I, acidic work-up. Reaction time: 3 h. Chromatography: hexane/EtOAc (3 : 1), yield: allylalcohol **24** (2.8 g, 7.4 mmol, 60%). $[\alpha]_D^{20}$ = +55.3° (c = 2.28; $CHCl_3$). IR: $\tilde{\nu}$ = 3445 (s, br), 2980 (s), 2934 (s), 2878 (s), 2249 (w), 1698 (s), 1606 (m), 1489 (s), 1437 (s), 933 (s) cm^{-1}. ^{1}H NMR: δ = 1.32 – 1.61 (m, 15 H; ketal–CH_3, *t*Bu–CH_3), 2.69 (s, br, 1 H; OH), 3.66 (m, 1 H; 5–H^A), 3.92 (m, 3 H; 1–H, 5–H^B), 4.45, 4.55 (2x m, 1 H; 4–H), 5.66 (t, J = 7.0 Hz, 1 H; 2–H), 5.88 (s, 2 H; OCH_2O), 6.46–6.78 (m, 3 H; Ar–CH). NOE analysis: OH ⇒ 1–H (7.8), 2–H (4.4), Ar–H^6 and Ar–H^2 (3.5); 5–H^A ⇒ 5–H^B (29.2), 2–H (0.8) Ar–H^2 and Ar–H^6 (7.3); 4–H ⇒ 5–H^B (6.7), 2–H (7.1), Ar–H^2 and Ar–H^6(15.8); 2–H ⇒ OH (3.4), 5–H^A (0.5), 1–H (5), 4–H (6.8); ^{13}C NMR: δ = 22.9, 26.2 (ketal–CH_3), 28.3 (*t*Bu–CH_3), 59.7 (C–1), 62.6, 62.8 (C–4), 67.2 (C–5), 79.8, 80.5 ($OCMe_3$), 94.2, 94.5 ($OCMe_2O$), 100.9 (OCH_2O), 108.0, 109.3, 122.3 (Ar–CH), 126.0, 126.5 (C–2), 131.1, 140.9, 141.4 (Ar–C), 146.8, 147.4 (C–3), 151.9, 152.3 (NC=O). MS (120 °C): m/z = 377 (4.4, M^+), 202 (20.7), 178 (13.8), 177 (39.8), 144 (19.3), 100 (23.2), 58 (12.0), 57 (100), 41 (14.3). HRMS: (M^+: $C_{20}H_{27}NO_6$) calc.: 377.1838, found: 377.1837. Analysis: $C_{20}H_{27}NO_6$ calc.: C/H = 8.83, found: C/H = 8.87

(1'*R*)-*E*-3-(2N,4O-*N*-*t*Butyloxycarbonyl-3,3-dimethyloxazolidinyl)-5-trimethylsilyl-2-penten-4-yn-1-ol (25): Reaction with α,β-unsaturated ester **23** (1.06 g, 2.7 mmol) following the standard procedure I, neutral work-up. Reaction time: 2 h. Chromatography: hexane/EtOAc (4 : 1), yield: allylalcohol **25** (0.6 g, 1.7 mmol, 63 %). $[\alpha]_D^{20}$ = –30.3° (c = 1.76; $CHCl_3$). IR: $\tilde{\nu}$ = 3451 (m, br), 2979 (s), 2146 (m), 1703 (s), 1478 (m), 1456 (m), 1366 (s), 1251 (s), 1173 (s), 844 (s) cm^{-1}. ^{1}H NMR: δ = 0.14 (s, 9 H; Si–CH_3), 1.29–1.64 (m, 15 H; ketal–CH_3, *t*Bu–CH_3), 2.39 (s, br, 1 H; OH), 3.88 (m, 1 H; 5'–H^A), 4.02 (m, 1 H; 5'–H^B), 4.24, 4.36 (2x m, 3 H; 5–H, 1'–H), 5.96 (m, 1 H; 2–H). NOE analysis: OH ⇒ 1–H and 1'–H (9.1), 2–H (2.6); 5'–H^A ⇒ OH (2.2), 5'–H^B (24.1), 2–H (0.6); 5'–H^B ⇒ 5'–H^A (28.7), 1'–H and 1–H (9.9); 2–H ⇒ OH (2.8), 5–H and 1'–H (18.6); 1–H and 1'H (4.24) ⇒ OH (2.6), 5'–H^B (15.9), 2–H (25); 1–H and 1'H (4.36) ⇒ OH (6.3), 5'–H^B (2.3), 2–H (8.6). ^{13}C NMR: δ = –0.5, –0.3 (3 C; Si–CH_3), 24.3, 26.1 (ketal–CH_3), 28.3 (*t*Bu–CH_3), 61.1 (C–1), 61.4 (C–1'), 67.5, 67.7 (C–5'), 79.9, 80.5 ($OCMe_3$), 94.2, 94.6 ($OCMe_2O$), 99.6, 123.6, 124.6 (3C; C≡C, C–3), 137.6, 137.7 (C–2), 151.7 (NC=O). MS (80 °C): m/z = 353 (1.0, M^+), 338 (1.1), 297 (14.2), 238 (20.7),

220 (30.7), 178 (17.5), 100 (27.8), 75 (21.2), 73 (46.4), 57 (100). HRMS: (M^+: $C_{18}H_{31}NO_4Si$) calc.: 353.2022, found: 353.2024.

(4*R*)-*E*-5-*t*Butyldimethylsilyloxy-3-(3,4-methylenedioxyphenyl)-4-trifluoracetamido-2-pentenoic-acid ethylester (26) and (4*R*)-*E*-4-amino-5-*t*butyldimethylsilyloxy-3-(3,4-methylenedioxyphenyl)-2-pentenoicacid ethylester (27): *Deprotection*: At 0 °C, the α,β-unsaturated ester **22** (1.53 g, 3.65 mmol) in CH_2Cl_2 (26 mL) was treated with trifluoroacetic acid (TFA, 2.83 mL). The mixture was stirred for 8 h, the temperature reached 20 °C. Then, the solvent was evaporated under reduced pressure, the residue was dissolved twice in $CHCl_3$ and the solvent was each distilled off. The crude aminoalcohol was dissolved in cold (0 °C) CH_2Cl_2 (18.4 mL) and treated subsequently with Et_3N (3.1 mL, 21.9 mmol) and TBSCl (1.98 g, 6.57 mmol, 50% in hexane). The mixture was stirred overnight, the temperature was raised to 20 °C. Then, H_2O (50 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3x 80 mL). After drying ($MgSO_4$) the solvent was removed and the crude mixture was purified by column chromatography with hexane/EtOAc (gradient 6 : 1 → 1 : 1) to give trifluoroacetamide **26** (0.57 g, 1.16 mmol, 32%) and aminoester **27** (0.95 g, 2.41 mmol, 66%). *Reduction*: $NaBH_4$ (0.72 g, 19 mmol) was suspended in dry EtOH (18.9 mL) at 0 °C. Trifluoroacetamide **26** (1.86 g, 3.8 mmol) in dry EtOH (18.9 mL) was added dropwise with stirring. After reaction overnight (the temperature reached 20 °C) aqueous saturated $NaHCO_3$ (25 mL) was added. The volume of the solution was reduced to the half. After extraction with Et_2O (4x 100 mL) the organic layers were dried (Na_2SO_4) and the solvent was removed. The crude amine was purified by column chromatography with hexane/EtOAc (1 : 1) to give the aminoester **27** (0.79 g, 2.01 mmol, 53%) as a clear oil.

Spectral data of **26**: $[\alpha]_D^{20}$ = +92.5° (c = 0.75; $CHCl_3$). IR: $\tilde{\nu}$ = 3424 (w), 3321 (m), 3076 (w), 2931 (s), 1728 (s), 1648 (w), 1490 (s), 1241 (s), 1175 (s), 1041 (s), 838 (s) cm^{-1}. ^1H NMR: δ = 0.04 (s, 6 H; Si–CH_3), 0.88 (s, 9 H; *t*Bu), 1.10 (t, *J* = 7.0 Hz, 3 H; Et–CH_3), 3.64 (m, 2 H; 5–H), 4.03 (q, *J* = 7.0 Hz, 2 H; Et–CH_2), 4.66 (m, 1 H; 4–H), 5.82 (s, 1 H; 2–H), 5.96 (s, 2 H; OCH_2O), 6.64–6.84 (m, 3 H; Ar–CH), 6.96 (d, br, *J* = 7.5 Hz, 1 H; NH). ^{13}C NMR: δ = –5.7 (2 C; Si–CH_3), 13.9 (Et–CH_3), 18.1 (Si–CMe_3), 25.6 (*t*Bu –CH_3), 56.7 (C–4), 60.2, 61.9 (C–5, Et–CH_2), 101.2 (OCH_2O), 108.2, 108.5 (Ar–CH), 118.9 (C–2), 121.5 (Ar–CH), 130.6, 147.6, 147.8 (Ar–C), 153.0 (C–3), 165.2 (C=O), 171.7 (N–CO). MS (180 °C): m/z = 489 (12.3, M^+), 433 (28.0), 432 (100), 89 (39.2), 86 (37.7), 84 (58.3), 77 (55.1), 75 (65.4), 73 (99.4), 44 (43.5). HRMS: (M^+: $C_{22}H_{30}F_3NO_6Si$) calc.: 489.1794, found: 489.1765.

Spectral data of **27**: $[\alpha]_D^{20}$ = +60.2° (c = 1.04; $CHCl_3$). IR: $\tilde{\nu}$ = 3387 (w), 2930 (s), 2857 (s), 1724 (s), 1644 (m), 1489 (s), 1239 (s), 1041 (s), 938 (m), 838 (s), 778 (s) cm^{-1}. ^1H NMR: δ = –0.03 (s, 6 H; Si–CH_3), 0.84 (s, 9 H; *t*Bu), 1.10 (t, *J* = 7.0 Hz, 3 H; Et–CH_3), 1.64 (s, br, 2 H; NH_2), 3.33 (dd, J = 6.5, 10.0 Hz, 1 H; 5–H^A), 3.56 (dd, J = 4.0, 10.0 Hz, 1 H; 5–H^B), 3.72 (m, 1 H; 4–H), 4.00 (q, *J* = 7.0 Hz, 2 H; Et–CH_2), 5.93 (s, 2 H; OCH_2O), 6.12 (s, 1 H; 2–H), 6.55–6.80 (m, 3 H; Ar–CH). ^{13}C NMR: δ = –5.5 (Si–CH_3), 14.0 (Et–CH_3), 18.1

(Si–C), 25.8 (*t*Bu –CH_3), 59.7 (C–4), 59.8 (Et–CH_2), 65.7 (C–5), 101.0 (OCH_2O), 107.9, 108.3 (Ar–CH), 118.3 (C–2), 121.0 (Ar–CH), 132.0, 147.3, 147.8 (Ar–C), 158.5 (C–3), 166.2 (C=O). MS (100 °C): m/z = 393 (11.6, M^+), 336 (31.7), 249 (15.2), 248 (100), 203 (14.8), 202 (44.7), 175 (9.6), 174 (53.4), 172 (15.2), 74 (7.4). HRMS: (M^+: $C_{20}H_{31}NO_5Si$) calc.: 393.1971, found: 393.1952.

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