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PAPER

Remote stereocontrol in reactions between 4- and 5-alkoxyalk-2-enylstannanes and 1-alkoxycarbonylimines and analogues: stereoselective approaches to novel α-amino acids†‡

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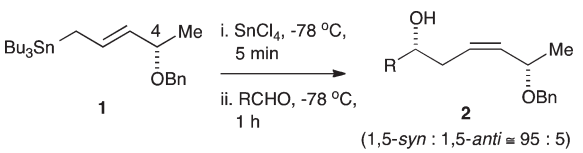
Reactions of the allyltin trichloride **45** generated from (4*S*)-4-benzyloxypent-2-enyl(tributyl)stannane **1** with imines prepared from glyoxylates proceed with useful levels of 1,5-stereocontrol in favour of (4*E*)-2,6-*anti*-2-(alkylamino)-6-benzyloxyhept-4-enoates **49**. This stereoselectivity, controlled by the chirality of the stannane, dominates over any intrinsic stereochemical bias of the imine although a small amount of matching and mis-matching was observed. The allyltin trichloride **77** prepared from (4*S*)-4-(*tert*-butyldimethylsilyloxy)pent-2-enyl(tributyl)stannane **52** reacts with 1-alkoxycarbonylimines with the opposite 1,5-stereoselectivity to give the (4*E*)-2,6-*syn*-diastereoisomers **79**. Matching and mismatching was more pronounced for tin(IV) chloride mediated reactions of (4*R*)-5-benzyloxy-4-methylpent-2-enyl (tributyl)stannane **80** with chiral 1-alkoxycarbonylimines but useful stereoselectivity in favour of (4*E*)-2,6-*syn*-2-alkyl- and arylthio-amino-7-benzyloxy-6-methylhept-4-enoates **177** was observed for reactions with achiral imines and similar, but reduced, stereoselectivity was observed for the 5-*tert*-butyldimethylsilyloxypentenylstannane **82**. However, excellent 1,5-stereocontrol in favour of the (4*E*)-2,6-*anti*-isomers **179** was found using the 4,5-bis-alkoxypent-2-enylstannane **106**. Modest (4*E*)-2,7-*anti*-stereoselectivity was observed in the analogous tin(IV) bromide mediated reactions of (*S*)-5-methoxy- and (*S*)-5-hydroxyhex-2-enyl(tributyl)stannanes (***S*)-123** and (***S*)-122** with achiral 1-alkoxycarbonylimines but in this series the intrinsic stereochemical bias of the imine controls the facial selectivity of reactions of chiral 1-alkoxycarbonylimines. Useful (4*E*)-2,6-*anti*-stereoselectivity was also observed in the tin(IV) chloride promoted reaction of the 4-benzyloxypent-2-enylstannane **1** with an oxime *O*-benzyl ether.

Introduction

Reactions between imines and organometallic reagents are widely employed for the stereoselective synthesis of amines[1] and useful diastereoselectivities have been found for reactions of imines that have chiral *N*-substituents.[2] Many procedures are also available for the enantioselective synthesis of amines from achiral imines using either chiral reagents or catalysts.[3] Reactions of allylic organometallic reagents,[4] including allylstannanes[5,6] and allylboranes,[7] have been widely studied in this context.

Tin(IV) halide mediated reactions of 4-, 5- and 6-alkoxyalk-2-enylstannanes with aldehydes proceed with useful levels of 1,5-, 1,6- and 1,7-stereocontrol.[8,9] For example the 4-benzyloxypent-2-enylstannane **1** on transmetalation with tin(IV) chloride generates an allyltin trichloride that reacts with aldehydes with excellent stereoselectivity in favour of (*Z*)-1,5-*syn*-5-benzyloxypent-3-enols **2**.[10] We here report on the tin(IV) halide mediated reactions of 4- and 5-alkoxy- and 5-hydroxy-alk-2-enylstannanes with imines, in particular with 1-alkoxycarbonyl imines, that proceed with useful levels of 1,5- and 1,6-stereocontrol.[11]



Results and discussion

Preliminary studies of reactions of alk-2-enyltin trichlorides and imines

The remote stereocontrol observed during reactions between alkoxyalk-2-enylstannanes and aldehydes involved participation

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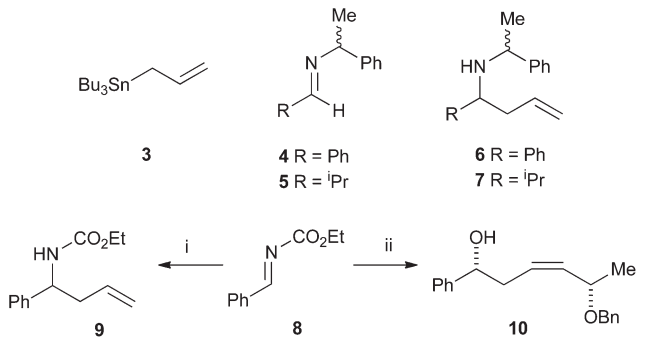
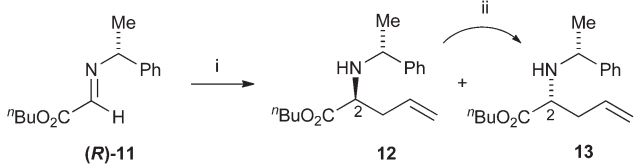
of allyltin trihalides at −78 °C formed by transmetalation of alk-2-enyl(tributyl)stannanes using tin(IV) chloride and bromide.[8,9] The reactivity of a series of imines towards such intermediates at −78 °C was therefore evaluated using prop-2-enyltin trichloride generated from prop-2-enyl(tributyl)stannane **3**.[6]

No imine addition products were found for the imines **4** and **5**, prepared from (±)-α-methylbenzylamine and either benzaldehyde or 2-methylpropanal, and prop-2-enyltin trichloride, although the expected adducts **6** and **7** were obtained using either titanium(IV) chloride or boron trifluoride diethyl etherate to promote the reaction with stannane **3**.[5a] The homoallylic carbamate **9** was obtained from the reaction between *N*-ethoxycarbonylimine **8** and prop-2-enyltin trichloride but this imine did not react with the allyltin trichloride generated from the 4-benzyloxypent-2-enyl(tributyl)stannane **1**. Instead the only product isolated was the (3*Z*)-1,5-*syn*-5-benzyloxy-1-phenylhex-3-enol **10**. This must have been derived from benzaldehyde generated by hydrolysis of the imine during the work-up of the reaction, see Scheme 1.[10]

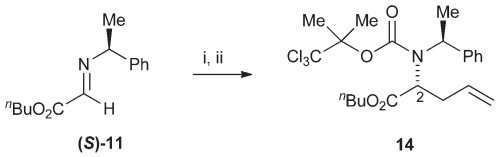


Scheme 1 Preliminary studies. Reagents and conditions: (i) **3**, $SnCl_4$, −78 °C, 15 min, **8**, −78 °C, 4 h, then satd. aq. NH_4Cl (92%); (ii) **1**, $SnCl_4$, −78 °C, 15 min, **8**, −78 °C, 4–12 h, then satd. aq. NH_4Cl (81–79%).

The successful reaction of the *N*-ethoxycarbonylimine **8** with prop-2-enyltin trichloride indicated that an electron withdrawing group on the imine could promote the reaction and so reactions of the imine (***R*)-11**[7] derived from butyl glyoxalate and (*R*)-α-phenylethylamine were investigated. This imine reacted with prop-2-enyltin trichloride efficiently and with a useful level of diastereoselectivity to give the 2-(alkylamino)pent-4-enoates **12** and **13**, ratio 93 : 7, see Scheme 2. The configurations of these products were assigned by comparison with authentic samples prepared by treatment of the imine **11** with 9-borabicyclo[3.3.1]nonane,[7] and were confirmed by the X-ray crystal structure‡ of the 2,2,2-trichloro-1,1-dimethylethoxycarbonyl derivative **14** of the major product from the prop-2-enyltin trichloride reaction with the enantiomeric imine (***S*)-11**, see Scheme 3 and Fig. 1. Of interest was the observation that the (2*S*)-2-(alkylamino)pentenoate **12** was the major product from the reaction of the imine (***R*)-11** with prop-2-enyltin trichloride, whereas the (2*R*)-epimer **13** was the dominant product from the reaction with 9-BBN.[7] Interestingly, the (2*S*)-2-(alkylamino)pentenoate **12** epimerized to give mainly the (2*R*)-epimer **13** on treatment with potassium *tert*-butoxide in tetrahydrofuran at −78 °C followed by an aqueous work-up.



Scheme 2 Stereoselectivity in the reaction between the chiral imine **11** and prop-2-enyltin trichloride. Reagents and conditions: (i) **3**, $SnCl_4$, −78 °C, 15 min, (***R*)-11**, −78 °C, 4 h, then satd. aq. NH_4Cl (90%; **12** : **13** = 93 : 7); (ii) KO^{t}Bu, THF, −78 °C, 10 min (88%; **12** : **13** = 15 : 85).



Scheme 3 Synthesis of the carbamate **14**. Reagents and conditions: (i) **3**, $SnCl_4$, −78 °C, 15 min, (***S*)-11**, −78 °C, 4 h, then satd. aq. NH_4Cl (88%; 93 : 7); (ii) $Cl_3CC(CH_3)_2OC(O)Cl$, 1,4-dioxane, K_2CO_3, heat under reflux, 16 h (90%).

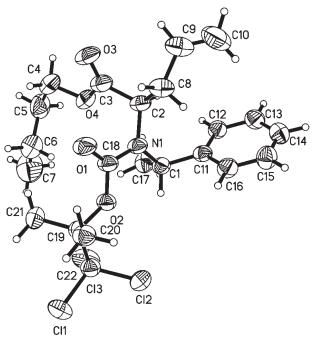
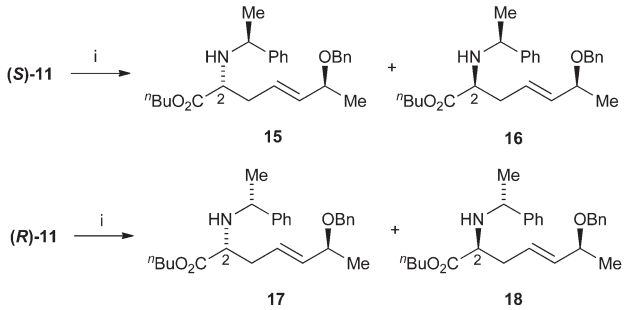


Fig. 1 Structure of the carbamate **14** as established by X-ray diffraction.

(*E*)-1,5-*anti*-Stereocontrol in reactions of 4-benzyloxypent-2-enyl(tributyl)stannane 1 and 1-alkoxycarbonylimines

Having established that the (*R*)-imine (***R*)-11** reacted efficiently with prop-2-enyltin trichloride, the reactions of this and analogous imines with the allyltin trichloride generated from the (4*S*)-4-benzyloxypent-2-enylstannane **1** were investigated. Optimum results were found when the reaction of the allyltin trichloride generated from the pent-2-enylstannane **1** and the (*S*)-imine (***S*)-11** were carried out at −45 °C for 12 h. Under these conditions, the (4*E*)-2,6-*anti*-2-(alkylamino)-6-benzyloxyhept-4-enoate **15** was the major product with only traces of its 2-epimer **16** being detected, **15** : **16** = 96 : 4. The reaction of the (*R*)-imine (***R*)-11** with the allyltin trichloride generated from stannane **1** was only slightly less stereoselective, the (4*E*)-2,6-*anti*-2-(alkylamino)-6-benzyloxyhept-4-enoate **17** being the major product together with *ca.* 10% of its epimer **18**, see Scheme 4.

Structures were initially assigned to the amino acid derivatives **15**/**16** and **17**/**18** using spectroscopic data. The coupling constants, $J_{4,5}$, between the vinylic protons for the alkenes **15**/**16** and **17**/**18** were *ca.* 16 Hz showing the presence of (*E*)-double-

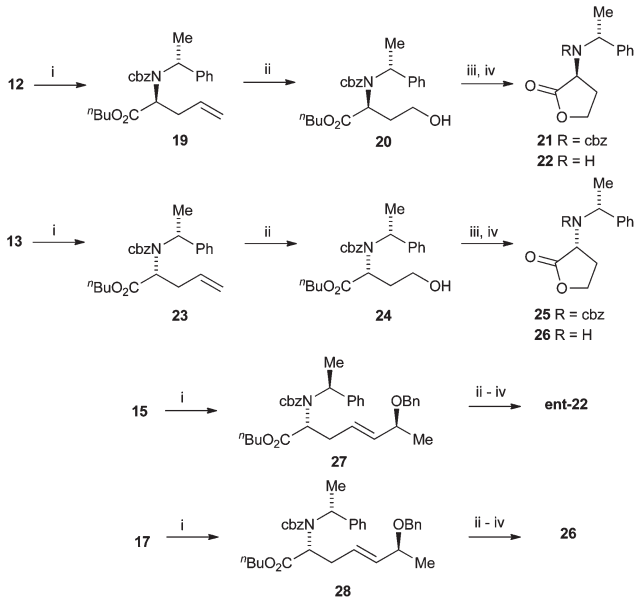


Scheme 4 Tin(IV) chloride mediated reactions of the alkenylstannane **1** with chiral imines. Reagents and conditions: (i) **1**, $SnCl_4$, 78 °C, 15 min, either (***S***)-**11** or (***R***)-**11**, −45 °C, 12 h, then satd. aq. NH_4Cl (**15**/**16**, 73%; **15** : **16** = 96 : 4; **17**/**18**, 72%; **17** : **18** = 92 : 8).

bonds. Of note, H(2) for the 1,3-*like*-epimers **13**, **16**, **17** was invariably more shielded than H(2) for the 1,3-*unlike*-epimers **12**, **15** and **18** (**13**, *δ*3.1, **12**, *δ*3.35; **16**, *δ*3.13, **15**, *δ*3.43; **17**, *δ*3.14, **18**, *δ*3.43), and this was found to be a reliable guide to the configuration at C(2) for all the 2-(α-methylbenzylamino) esters prepared during this work. However, to confirm the stereochemical assignments at C(2), correlation was made using the lactones **22** and **26** prepared from the 2-(alkylamino)pentenoates **12** and **13**, see Scheme 5. Thus, following cbz-protection of the amino esters **12** and **13**, ozonolysis of the resulting carbamates **19** and **23** with a reductive work-up gave the alcohols **20** and **24**. Cyclisation in acidic methanol then gave the lactones **21** and **25** and these were *N*-deprotected to the amines **22** and **26** using transfer hydrogenolysis, see Scheme 5. These amines were easily distinguished by ^{1}H NMR and the structure of the 1,3-*like*-cbz-aminolactone **25** was confirmed by a single crystal X-ray structure determination, see Fig. 2.‡ Following this sequence, the major product from the reaction of the imine (***S***)-**11** with the stannane **1** gave the enantiomeric 1,3-*unlike* aminolactone **ent-22** and the aminolactone **26** was obtained from the major product from the reaction between the imine (***R***)-**11** and the stannane **1**, so confirming the assigned configurations.

The reactions of the allyltin trichloride generated from the (*S*)-4-benzyloxypent-2-enylstannane **1** with the imines (***S***)-**11** and (***R***)-**11** both proceed with useful 1,5-stereoselectivity in favour of the (4*E*)-2,6-*anti*-hept-4-enoates **15** and **17**. These imines, as judged from the reaction with the achiral prop-2-enyltin trichloride, would prefer to give 2-(α-methylbenzylamino)alk-4-enoates with the 1,3-*unlike* configuration between C(2) and the (α-methylbenzylamino) substituent, *e.g.* **12**. This was consistent with the small degree of matching and mismatching observed for the reactions of the enantiomeric imines (***S***)- and (***R***)-**11** with the (*S*)-4-benzyloxpent-2-enylstannane **1**, 96 : 4 *vs.* 92 : 8, but overall the stereoselectivities of these reactions were primarily controlled by the allyltin trichloride.

It now remained to investigate the stereoselectivities of tin(IV) chloride mediated reactions of the 4-benzyloxypent-2-enylstannane **1** with achiral 1-alkoxycarbonylimines. The reactions of the *o*-nitrophenylsulfanylimine **29**[12] and the two imines **32** and **35** with the allyltin trichloride generated from the (*S*)-4-benzyloxypent-2-enylstannane **1** were found to be usefully stereoselective (*ca.* 90 : 10) with the (*E*)-2,6-*anti*-2-amino-6-benzyloxyhept-4-enoates **30**, **33** and **36** being the major products, see Scheme 6.



Scheme 5 Stereochemical correlations. Reagents and conditions: (i) BnOCOCl, K_2CO_3, $CHCl_3$, heat, 16 h (83–94%); (ii) (a) O_3, MeOH, −78 °C, 1.5 h, then Me_2S, r.t., 1 h (b) $NaBH_4$, MeOH, 0 °C – r.t., 30 min; (iii) MeOH, aq. HCl, 16 h (72–86% two steps); (iv) MeOH, NH_4O_2CH, 10% Pd/C, r.t., 30 min (71–85%).

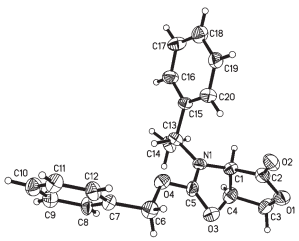
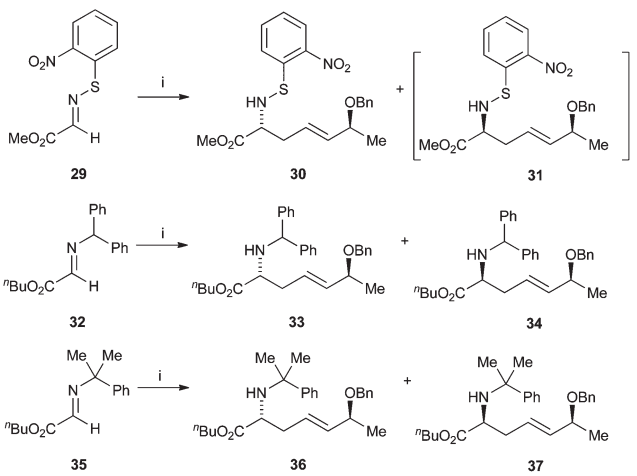
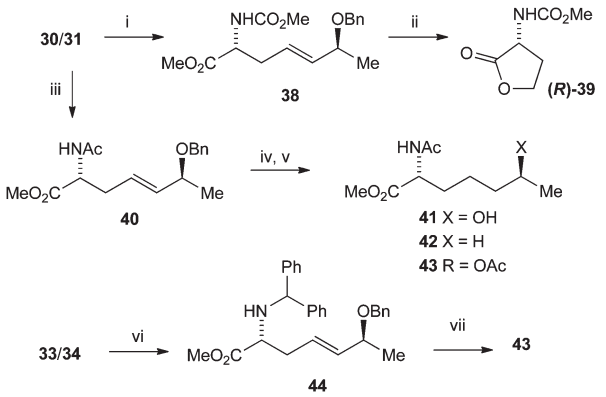


Fig. 2 Structure of the 2-(alkylamino)lactone **25** as established by X-ray diffraction.



Scheme 6 Tin(IV) chloride mediated reactions of the alkenylstannane **1** with achiral imines. Reagents and conditions: (i) **1**, 78 °C, $SnCl_4$, 15 min, either **29**, **32**, or **35**, −45 °C, 12 h, then satd. aq. NH_4Cl (**30**/**31**, 87%, **30** : **31** = 90 : 10; **33**/**34**, 86%; **33** : **34** = 90 : 10; **36**/**37**, 78%; **36** : **37** = 91 : 9).



Scheme 7 Assignment of configuration to the products from the reactions of stannane **1** with achiral imines. Reagents and conditions: (i) (a) HCl, MeOH, r.t., 2 h, (b) K_2CO_3, MeO_2CCl, $CHCl_3$, r.t., 16 h (87%); (ii) (a) O_3, MeOH, −78 °C, 90 min, Me_2S, r.t., 1 h (b) $NaBH_4$, 0 °C – r.t., 30 min (c) AcOH, $CHCl_3$, reflux, 16 h (73%); (iii) (a) HCl, MeOH, r.t., 2 h, (b) Ac_2O, Et_3N, DMAP, CH_2Cl_2, r.t., 16 h (82%); (iv) HCO_2H, MeOH, 10% Pd/C, r.t., 16 h (**41**, 79%; **42**, 5%); (v) Ac_2O, Et_3N, DMAP, CH_2Cl_2, r.t.,16 h (95%); (vi) K_2CO_3, MeOH, H_2O, heat under reflux, 16 h, then CH_2N_2, Et_2O, r.t., 30 min (91%); vii, (a) HCO_2H, MeOH, 10% Pd/C, r.t., 16 h (b) Ac_2O, Et_3N, DMAP, CH_2Cl_2, r.t., 16 h (80%).

Structures were assigned to the products in Scheme 6 on the basis of spectroscopic data and by correlation with known compounds, see Scheme 7. ^{1}H NMR coupling constants between the vinylic protons confirmed their (*E*)-configurations. Only one isomer was detected from the reaction of the sulfanylimine **29**[13] and stannane **1** and this was correlated with the methoxycarbonyl derivative (***R***)-**39**[14] of (*R*)-homoserine lactone by conversion into the carbamate **38**, ozonolysis with a reductive work up, and lactonisation of the resulting hydroxyester. This established the (2*R*)-configuration of the major product **30** and, as the carbamate **39** had an e.e. of *ca.* 80%, the stereoselectivity of the reaction between stannane **1** and the sulfanylimine **29** was estimated to be *ca.* 90 : 10. The product mixture from the sulfanylimine **29** was also converted into the 6-acetoxy-2-acetamidoheptanoate **43** by replacement of the group on nitrogen to give the acetamide **40**, hydrogenation with hydrogenolysis to give the alcohol **41** together with a small amount of the *O*-hydrogenolysis product **42**, and *O*-acetylation. Comparison of the 2,6-*anti*-ester-amide **43** with its *syn*-diastereoisomer **73** prepared later, showed that about 10% of the *syn*-diastereoisomer was present so confirming the ratio of the 2,6-*anti*- to 2,6-*syn*-products **30** : **31** to be *ca.* 90 : 10.

The benzhydryl products **33** and **34** could not be separated but were distinguishable by ^{1}H NMR. Following ester exchange, the methyl ester **44** was taken through to the acetamidoheptanoate **43** by hydrogenation and hydrogenolysis followed by *O*- and *N*-acetylation. This confirmed that the major product from the reaction of the alkenylstannane **1** with the *N*-benzhydrylimine **32** had been the 2,6-*anti*-product **33** as shown. The 2,6-*anti*-configuration was assigned to the major product **36** from the reaction of the stannane **1** with the dimethylbenzylimine **35** by analogy, the ratio **36** : **37** being determined by ^{1}H NMR.

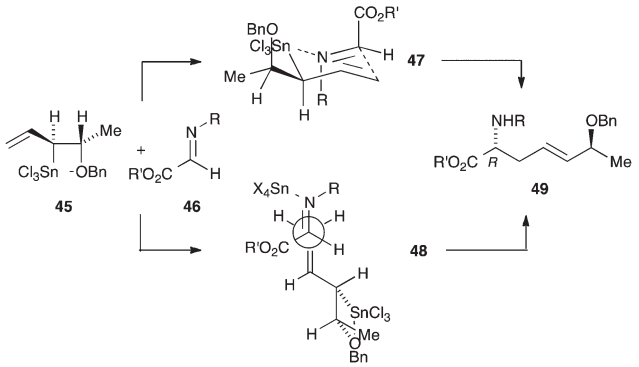


Fig. 3 Cyclic and open-chain transition structures for the reaction of the allyltin trichloride **45** with achiral imines.

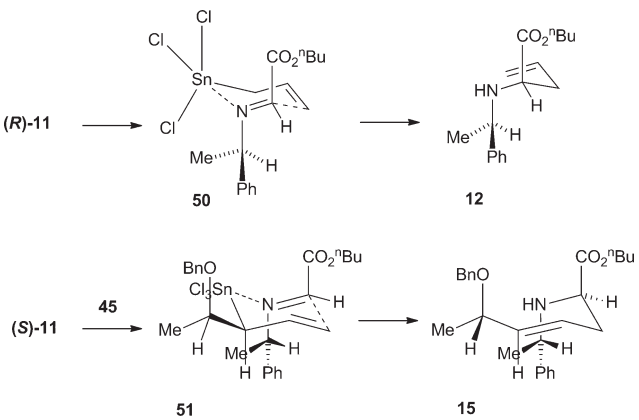


Fig. 4 Cyclic transition structures for reactions of allyltin trichlorides with chiral imines (***R***)-**11** and (***S***)-**11**.

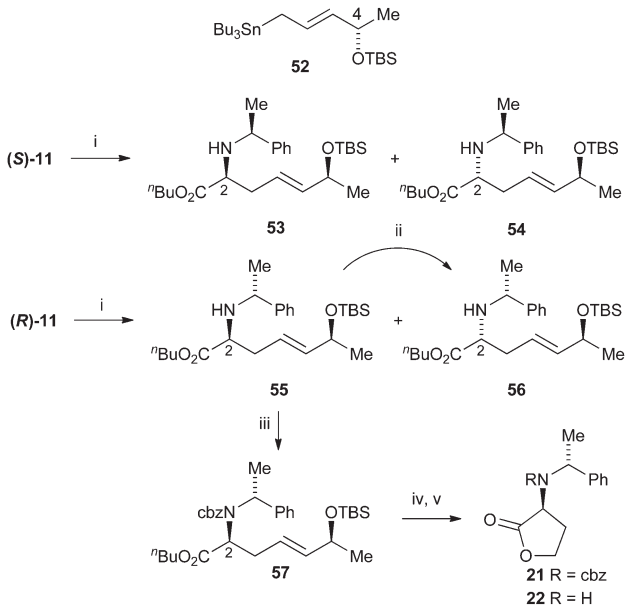
The tin(IV) chloride promoted reactions of the 4-benzyloxypentenylstannane **1** with achiral imines proceed to give (*E*)-2,6-*anti*-2-amino-6-benzyloxyhept-4-enoates as observed for the chiral imines (***R***)- and (***S***)-**11**. This stereoselectivity differs from that observed for the analogous reactions with aldehydes where (3*Z*)-alk-3-enols **2** were obtained as the dominant products.

The mechanisms of these reactions have not been studied in detail but, following trapping experiments,[15] it is believed that transmetalation of stannane **1** by tin(IV) chloride at −78 °C, generates the reactive allyltin trichloride **45** stereoselectively by intramolecular delivery of the trichlorotin group by the oxygen of the benzyloxy substituent.[8,9] The formation of the (4*E*)-2,6-*anti*-products **49** from the reactions with the 2-alkoxycarbonylimines **46** and the allyltin trichloride **45** would then be consistent with participation of either the cyclic 6-membered, chair-like transition structure **47** or the open-chain process **48**. In both cases the intermediate (3*S*,4*S*)-allyltin trichloride **45** is reacting with the *si* face of the imine to give the product with the (*R*)-configuration at C(2) as the major product with concomitant formation of the (*E*)-double-bond, see Fig. 3.[16]

The cyclic transition structure **50** is consistent with the preferred formation of the amine **12** from the reaction of the chiral imine (***R***)-**11** with prop-2-enyltin trichloride. The analogous cyclic transition structure **51** is consistent with the matching seen in the reaction between the chiral imine (***S***)-**11** and the allyltin trichloride **45**,[18] see Fig. 4.

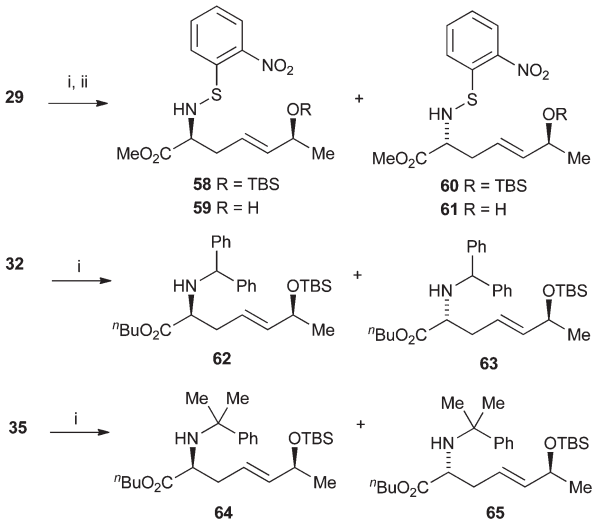
1,5-*syn*-Stereocontrol using 4-(*tert*-butyldimethysilyloxy)pent-2-enyl(tributyl)stannane (52)

The 4-(*tert*-butyldimethylsilyloxy)pent-2-enylstannane **52** shows reversed, albeit somewhat reduced, stereoselectivity in tin(IV) chloride mediated reactions with aldehydes compared with the 4-(benzyloxy)pent-2-enylstannane **1**.[19] Therefore, it was of interest to investigate analogous reactions of stannane **52** with 1-alkoxycarbonylimines. The tin(IV) chloride mediated reactions of the stannane **52** with the chiral imines (***S*)-11** and (***R*)-11**, proceeded with modest stereoselectivities, but unlike the reactions with the 4-benzyloxystannane **1**, the (*E*)-2,6-*syn*-diastereoisomers **53** and **55** were the major products, see Scheme 8. The stereoselectivity of the reaction with the (*R*)-imine (***R*)-11** was slightly better than that observed for the (*S*)-imine (***S*)-11**, consistent with the preference of the chiral imines to form 1,3-*unlike*-epimers, *vide supra*.



Scheme 8 Reactions of the 4-silyloxypent-2-enylstannane **52** with chiral imines. Reagents and conditions: (i) **52**, 78 °C, $SnCl_4$, 15 min, either (***S*)-11** or (***R*)-11**, −45 °C, 12 h, then satd. aq. NH_4Cl (**53**/**54**, 76%; **53** : **54** = 66 : 34; **55**/**56**, 93%; **55** : **56** = 73 : 27); (ii) KO^{t}Bu, THF, −78 °C, 10 min (86%; **55** : **56** = 15 : 85); (iii) BnOCOCl, K_2CO_3, $CHCl_3$, heat, 16 h (79%); (iv) (a) O_3, MeOH, −78 °C, 1.5 h, then Me_2S, r.t., 1 h (b) $NaBH_4$, MeOH, 0 °C – r.t., 30 min (c) MeOH, aq. HCl, 16 h (**21**, 48% 3 steps); (v) MeOH, ammonium formate, 10% Pd/C, r.t., 30 min (66%).

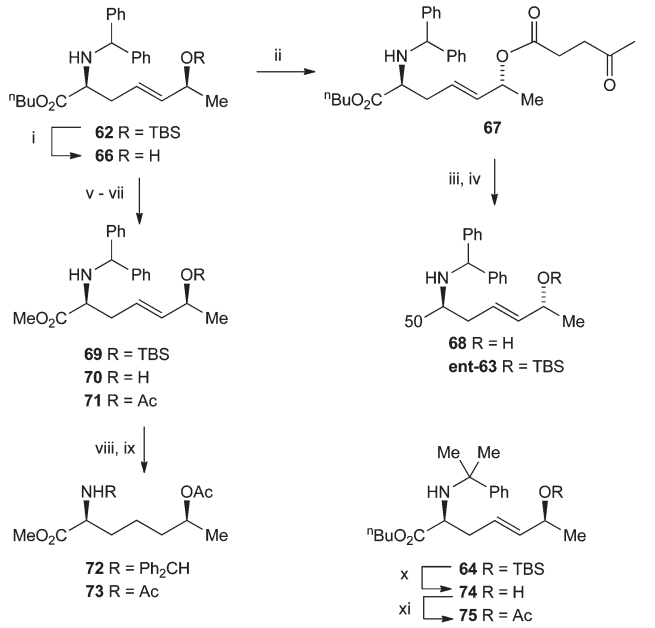
Structures were assigned to the products **53–56** on the basis of spectroscopic data. In all cases the coupling between the vinylic protons, $J_{4,5}$, was *ca.* 15 Hz, consistent with the (*E*)-configuration assigned to the double-bonds. The configuration at C(2) was assigned on the basis of the increased shielding of H(2) for the 1,3-*like*-epimers **53** and **56** (**53**, δ3.00, **54**, δ3.29; **55**, δ3.29, **56**, δ3.01) and was confirmed for the major isomer **55** from the reaction with the (*R*)-imine (***R*)-11** by correlation with the lactone **22**, see Scheme 8. Treatment of the 1,3-*unlike* epimer **55** with potassium *tert*-butoxide also initiated epimerisation to give more of the 1,3-*like* epimer **56**.



Scheme 9 Reactions of the 4-(*tert*-butyldimethylsilyloxy)pent-2-enylstannane **52** with achiral imines. Reagents and conditions: (i) **52**, $SnCl_4$, 78 °C, 15 min, add imine, −45 °C, 12 h, then satd. aq. NH_4Cl (**58**/**60**, 85%; **58** : **60** = 75 : 25; **62**/**63**, 91%; **62** : **63** = 75 : 25; **64**/**65**, 74%; **64** : **65** = 75 : 25); (ii) TBAF, THF, 0 °C 12 h (79%).

The tin(IV) chloride mediated reactions of the 4-(*tert*-butyldimethylsilyloxy)pent-2-enylstannane **52** with the achiral imines **29**, **32** and **35** were also examined, see Scheme 9. In all cases, an approximately 3 : 1 mixture of products was obtained in favour of the (*E*)-1,5-*syn*-diastereoisomers **58**, **62** and **64**.

Structures were initially assigned to the products **58**, **60**, **62–65** by analogy with the corresponding reactions of stannane **52** with the chiral imines (***S*)-11** and (***R*)-11**. The epimeric products **58**/**60**, **62**/**63** and **64**/**65** could not be separated. In the *N*-diphenylmethyl series, the two products **62** and **63** were distinguishable by ^{1}H NMR and were shown to be epimers by conversion into a 3 : 1 mixture of ***ent*-63** and ***ent*-62** by desilylation followed by a Mitsunobu inversion using levulinic acid. Reductive cleavage of the resulting levulinate **67** using sodium borohydride and silylation of the free hydroxyl group then gave ***ent*-63** (containing *ca.* 25% of its 2-epimer ***ent*-62**) whose ^{1}H NMR spectrum corresponded to that of the minor product from the allylstannane reaction, see Scheme 10. To confirm the configuration at C(2) of the major product **62**, the 3 : 1 mixture of epimers **62** and **63** was saponified and re-esterified using diazomethane to give the methyl ester **69**. Following desilylation and conversion of the alcohol **70** into the acetate **71**, hydrogenation/hydrogenolysis and *N*-acetylation gave the 2,6-*syn*-2-acetamido-6-acetoxyheptanoate **73** (still containing *ca.* 25% of its 2-epimer), see Scheme 10. Comparison with the 2,6-*anti*-epimer **43** (see Scheme 7) confirmed that the major product from the reaction of stannane **52** with imine **32** was indeed the 2,6-*syn*-diastereoisomer **62**. Structures were assigned to the products **58** and **60** from the reaction with the *N*-phenylsulfanylimine **29** by analogy. Their ratio and double-bond geometry were established by ^{1}H NMR and confirmed by desilylation and separation of the alcohols **59** and **61**. The products **64** and **65** from the reaction of stannane **50** with the imine **35** were distinguishable by ^{13}C NMR and the major acetate **75**, prepared by desilylation and *O*-acetylation, was shown to be an (*E*)-alkene by ^{1}H NMR.



Scheme 10 Confirmation of the structures of the products from the reactions of stannane **52** with achiral imines. Reagents and conditions: (i) TBAF, THF, r.t., 6 h (96%); (ii) Ph_3P, levulinic acid, THF, DEAD, r.t., 16 h (83%); (iii) $NaBH_4$, MeOH, 0 °C–r.t., 30 min (90%); (iv) TBSCl, imid., CH_2Cl_2, r.t., 16 h (*ca.* 100%); (v) K_2CO_3, MeOH, H_2O, heat under reflux, 16 h, then CH_2N_2, ether, r.t., 30 min (98%); (vi) TBAF, THF, r.t., 16 h (97%); (vii) Ac_2O, Et_3N, DMAP, CH_2Cl_2, 16 h (99%); (viii) $TsNHNH_2$, DME, NaOAc, heat under reflux, 16 h (99%); (ix) HCO_2H, MeOH, 10% Pd/C, r.t., 16 h, then Ac_2O, Et_3N, DMAP, CH_2Cl_2, r.t., 16 h (85%); (x) TBAF, THF, r.t., 4 h (86%); (xi) Ac_2O, Et_3N, DMAP, CH_2Cl_2, r.t., 16 h (94%).

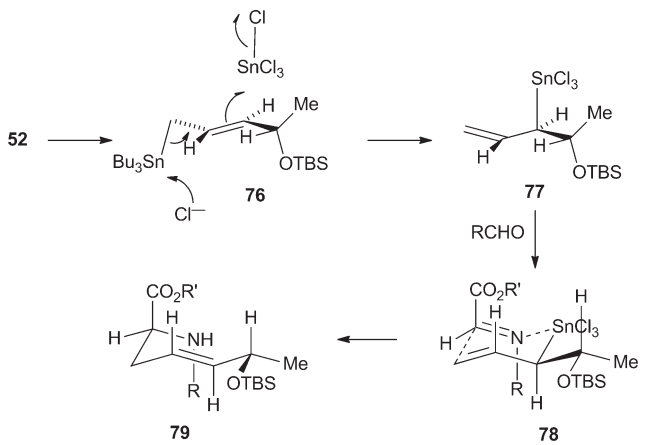
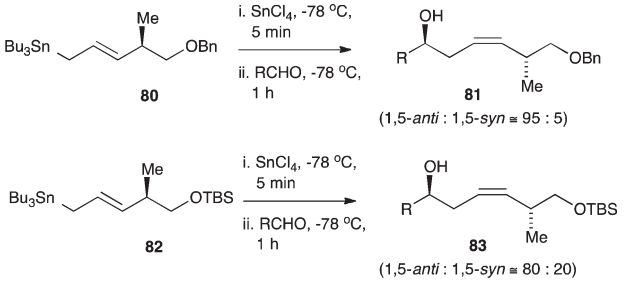


Fig. 5 2,6-*syn*-Stereoselectivity in reactions of the 4-(*tert*-butyldimethylsilyloxy)pent-2-enylstannane **52** and imines.

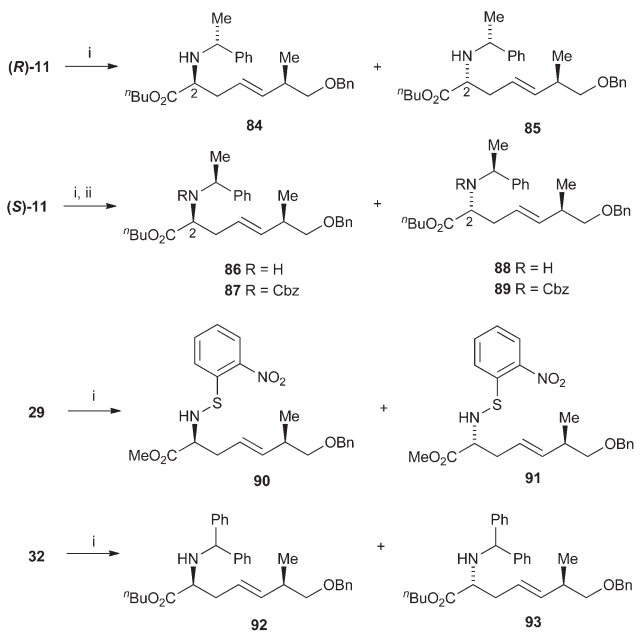
The preferred formation of the 2,6-*syn*-products from the tin(IV) chloride promoted reactions of the 4-(*tert*-butyldimethylsilyloxy)pent-2-enylstannane **52** and imines is consistent with participation of the non-coordinated allyltin trichloride **77** formed by transmetalation of the tributylstannane **52** on the less hindered face of the double-bond away from the allylic *O*-TBS substituent in conformation **76** in which the allylic methyl group is in the less hindered *exo*-position, see Fig. 5. Reaction of this allyltin trichloride with imines, *e.g. via* the cyclic transition structure **78**, would lead to the observed overall 2,6-*syn*-stereoselectivity.

(*E*)-1,5-*syn*-Stereocontrol using 5-benzyloxy- and 5-(*tert*-butyldimethylsilyloxy)-4-methylpent-2-enyl(tributyl)stannanes 80 and 82 with imines

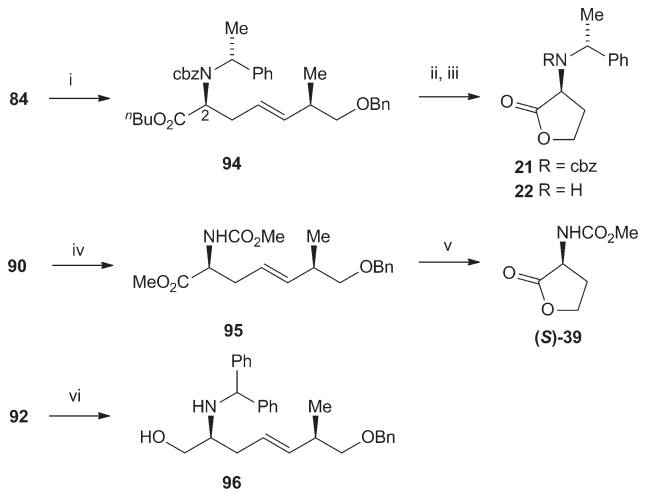
Transmetalation of the (*R*)-5-benzyloxy-4-methylpent-2-enyl (tributyl)stannane **80** with tin(IV) chloride generates an allyltin trichloride that reacts with aldehydes with useful diastereoselectivity in favour of the (*Z*)-1,5-*anti*-diastereoisomers **81**.[8] In this series, the corresponding 5-(*tert*-butyldimethylsilyloxy)pentenylstannane **82** also gives rise to the (*Z*)-1,5-*anti*-diastereoisomers **83** but with somewhat reduced stereoselectivity.[19] The stereoselectivities of reactions of these pent-2-enylstannanes with imines were investigated.



Following the usual procedure, the 5-benzyloxy-4-methylpent-2-enylstannane **80** was transmetalated using tin(IV) chloride and the allylin trichloride so formed allowed to react with the chiral imines (***R*)-11** and (***S*)-11** and with the achiral imines **29**



Scheme 11 Reactions of the 5-benzyloxy-4-methylpent-2-enylstannane **80** with imines. Reagents and conditions: (i) **80**, 78 °C, $SnCl_4$, 15 min, add imine, −45 °C, 12 h, then satd. aq. NH_4Cl (**84**/**85**,76%; **84** : **85** = 95 : 5; **86**/**88**, 96%; **86** : **88** = 60 : 40; **90**/**91**, 74%; **90** : **91** = 95 : 5; **92**/**93**, 78%; **92** : **93** = 95 : 5); (ii) BnOC(O)Cl, K_2CO_3, $CHCl_3$, heat under reflux 16 h (84%).

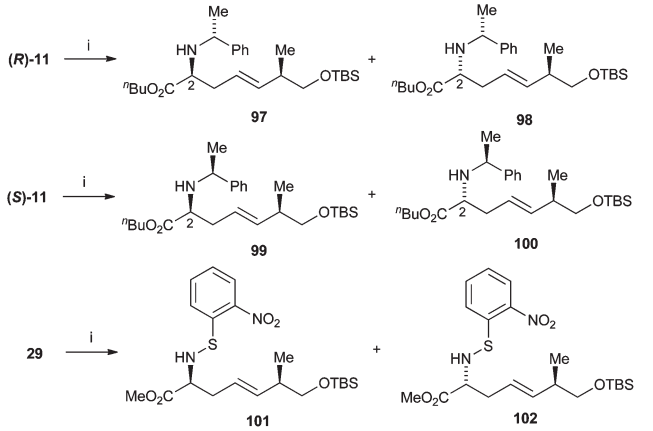


Scheme 12 Confirmation of the structures of the products from reactions of imines with the pent-2-enylstannane **80**. Reagents and conditions: (i) BnOC(O)Cl, K_2CO_3, $CHCl_3$, heat under reflux, 16 h (87%); (ii) (a) O_3, MeOH, −78 °C, 90 min, Me_2S, r.t., 1 h (b) $NaBH_4$, 0 °C to r.t., 30 min (80%) (c) aq. HCl, MeOH, r.t., 16 H (80%); (iii) ammonium formate, 10% Pd/C, MeOH, r.t., 3 min (82%); (iv) HCl, MeOH, r.t., 2 h, MeOC(O)Cl, K_2CO_3, $CHCl_3$, r.t., 16 h (77%); (v) (a) O_3, MeOH, −78 °C, 90 min., Me_2S, r.t., 1 h, (b) $NaBH_4$, r.t., 30 min (c) glacial HOAc, $CHCl_3$, heat under reflux 16 h (62%); (vi) DIBAL-H, CH_2Cl_2, −78 °C, to r.t., 1 h (92%).

and **32**, see Scheme 11. Useful stereoselectivities were observed for the matched reaction with the (*R*)-imine (***R*)-11** and with the achiral imines **29** and **32** in favour of the (*E*)-2,6-*syn*-hept-4-enoates **84**, **90** and **92**, but only modest stereoselectivity, albeit still in favour of the (*E*)-1,5-*syn*-diastereoisomer **86**, was observed for the mismatched reaction with the (*S*)-imine (***S*)-11**.

The C(2)-configurations of the products **84–86** and **88** from the chiral imines (***R*)-11** and (***S*)-11** were initially assigned using the relative chemical shifts of H(2). The C(2) configuration of the major product **84** from the (*R*)-imine (***R*)-11** was confirmed by cbz-protection of the 2-amino group and ozonolysis of the carbamate **94** with a reductive work up followed by lactonisation to the 2-amidolactone **21**. This was converted into the 2-(alkylamino)lactone **22** prepared earlier, see Scheme 12. Structures were assigned to the products **86** and **88** from the (*S*)-imine (***S*)-11** by their H(2) chemical shifts, these products being more easily separated as their *N*-cbz-derivatives **87** and **89**. The major product **90** from reaction of stannane **80** with the *N*-sulfanylimine **29** was converted into the carbamate **95**. Ozonolysis with a reductive work up and lactonisation then gave the lactone (***S*)-39**[14] so confirming its configuration at C(2). The structure of the major product isolated from the achiral imine **32** was assigned by analogy, its double-bond configuration being established by the vinylic coupling constant of 15.5 Hz observed for the DIBAL-H reduction product **96**, see Scheme 12.

Following the usual procedure, the 5-(*tert*-butyldimethylsilyloxy)-4-methylpent-2-enylstannane **82** was transmetalated using tin(IV) chloride and the allyltin trichloride so formed allowed to react with the chiral imines (***R*)-11** and (***S*)-11** and the achiral imine **29**, see Scheme 13. Useful stereoselectivity was observed for the matched reaction with the (*R*)-imine (***R*)-11** in favour of



Scheme 13 Reactions of the 5-(*tert*-butyldimethylsilyloxy)-4-methylpent-2-enylstannane **82** with imines. Reagents and conditions: (i) **82**, $SnCl_4$, 78 °C, 15 min, add imine, −45 °C, 12 h, then satd. aq. NH_4Cl (**97**/**98**, 74%; **97** : **98** = 95 : 5; **99**/**100**, 80%; **99** : **100** = 75 : 25; **101**/**102**, 77%; **101** : **102** = 80 : 20).

the (*E*)-2,6-*syn*-hept-4-enoate **97** but only modest stereoselectivities, albeit still in favour of the (*E*)-1,5-*syn*-diastereoisomers **99** and **101** were observed for the mismatched reaction with the (*S*)-imine (***S*)-11** and for the reaction with the achiral imine **29**. The C(2) configurations of the products **97–100** prepared from the chiral imines (***R*)-11** and (***S*)-11** were assigned using the relative chemical shifts of H(2), and the structures of the products **101** and **102** from the achiral imine **29** were assigned by analogy.

These reactions of the 5-benzyloxy- and 5-(*tert*-butyldimethylsilyloxy)-4-methylpent-2-enylstannanes **80** and **82** with imines are consistent with transmetalation generating the allyltin trichlorides **103** (R = Bn, TBS).[8,19] These intermediates can then react with the imines *via* the cyclic transition structure **104** to give the (*E*)-2,6-*syn*-products **105**, see Fig. 6. An open chain transition structure analogous to **48** would give the same overall result. Unlike, the 4-alkoxypent-2-enylstannanes **1** and **52**, it would appear that the 5-benzyloxy- and 5-(*tert*-butyldimethylsilyloxy)pentenylstannanes **80** and **82** are transmetalated with the same diastereofacial selectivity to give the (3*R*,4*S*)-allyltin trichlorides **103**, albeit more stereoselectively from the 5-benzyloxystannane **80**. This is consistent with the preferred formation of the (*Z*)-1,5-*anti*-products **81** and **83** in their tin(IV) chloride promoted reactions with aldehydes.

(*E*)-1,5-*anti*-Stereocontrol using (*S*)-4-(2-trimethylsilylethoxymethoxy)-5-(*tert*-butyldimethylsilyloxy)pent-2-enyl(tributyl)stannane 106

It was of interest to investigate the reactions of dialkoxyalk-2-enylstannanes with imines to see if these could proceed with useful levels of remote stereocontrol. Tin(IV) chloride mediated reactions of the 4-(trimethylsilylethoxymethoxy)-5-(*tert*-butyldimethylsilyloxy)pent-2-enylstannane **106** with aldehydes have been found to proceed with useful levels of stereoselectivity in favour of the (*Z*)-1,5-*syn*-distereoisomers **107** and these products have been used in stereoselective syntheses of 2,6-disubstituted

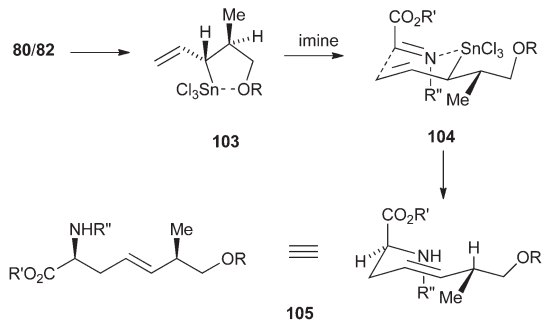
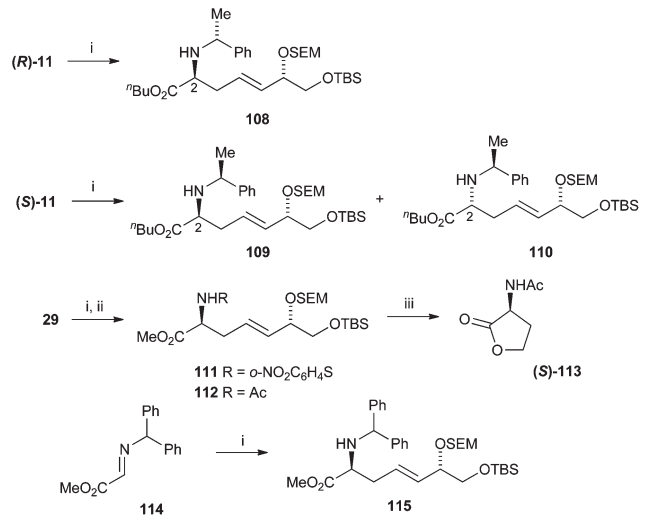
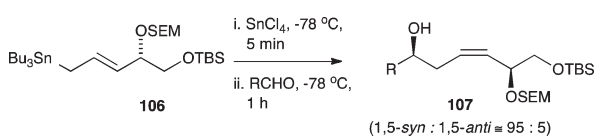


Fig. 6 Cyclic transition structures for the reactions of allyltin trichlorides generated from the allylstannanes **80** and **82** with imines.

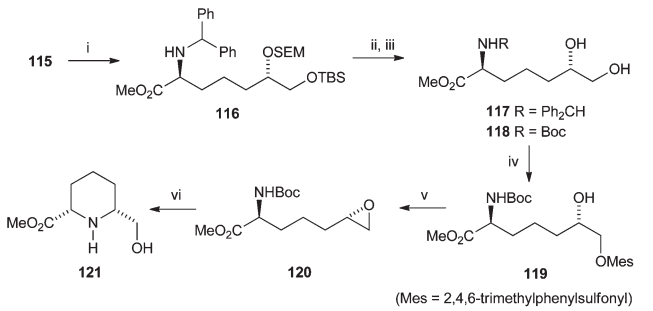


Scheme 14 Reactions of the stannane **106** with imines. Reagents and conditions: (i) **106**, 78 °C, $SnCl_4$, 15 min, add imine, −45 °C, 12 h, then satd. aq. NH_4Cl (**108**, 72%; **109**/**110**, 68%; **109** : **110** = 96 : 4; **111**, 81%; **115**, 72%); (ii) Ac_2O, Et_3N, DMAP, $CHCl_3$, heat under reflux, 16 h (74%); (iii) (a) O_3, MeOH, −78 °C, 90 min., Me_2S, r.t., 1 h (b) $NaBH_4$, 0 °C – r.t., 30 min (c) glacial HOAc, $CHCl_3$, heat under reflux 16 h (60%).

tetrahydropyrans.[20] Reactions of the stannane **106** with 1-alkoxycarbonyl imines were therefore investigated.



It was found that the tin(IV) chloride mediated reactions of the stannane **106** with both chiral and achiral aldehydes proceeded with excellent stereocontrol in favour of (*E*)-2,6-*anti*-2-(alkylamino)hept-4-enoates **108**, **109**, **111** and **115**, see Scheme 14. For the matched reaction with the (*R*)-imine (***R*)-11** and for the reactions with the achiral imines **29** and **114** the overall stereoselectivity was greater than 98 : 2 in favour of the (4*E*)-2,6-*anti*-diastereoisomers and other products were not detected. For the reaction with the mismatched imine (***S*)-11**, a minor product assumed to be the (4*E*)-1,5-*syn*-epimer **110** was detected, but even in this case the stereoselectivity was *ca.* 96 : 4.



Scheme 15 Synthesis of a pipecolic acid derivative. Reagents and conditions: (i) $TsNHNH_2$, DME, NaOAc, heat under reflux 18 h (90%); (ii) HCl, MeOH, r.t., 2 h (*ca.* 100%); (iii) (a) HCO_2H, MeOH, 10% Pd/C, r.t., 16 h (b) Boc-ON, Et_3N, CH_2Cl_2, heat under reflux, 3 h (70%); (iv) 2-mesitylenesulfonyl chloride, py., 0 °C, 16 h (83%); (v) KO^{t}Bu, THF, −78 °C, 5 min (83%); (vi) TFA, $CHCl_3$, r.t., 2 h (68%).

Structures were assigned to the products **108–110** from the chiral imines by analogy with earlier work and were consistent with the H(2) chemical shifts for the *like*- and *unlike*-1,3-epimers **109** and **110**. The C(2) configuration of the product **111** from the achiral imine **29** was established by ozonolysis of the acetamide **112** prepared from the sulfanamide **111** and conversion of the ozonolysis product into the known (*S*)-*N*-acetyl homoserine lactone (***S*)-113**,[21] see Scheme 14. The structure of the product **115** from the achiral imine **114** was assigned by analogy.

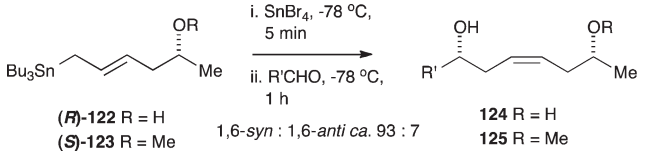
The preference for formation of the (*E*)-2,6-*anti*-products **108**, **109**, **111** and **115** in these reactions follows the stereoselectivity observed for the reactions between the 4-benzyloxystannane **1** and 1-alkoxycarbonyl imines. Analogous intermediates may be involved, see Fig. 3 and 4.

To show the potential of these products for synthesis, the product **115** from the benzhydryl imine **114** was converted into the methyl 6-(hydroxymethyl)pipecolinate **121**, see Scheme 15. Thus, diimide reduction gave the heptanoate **116** that was deprotected and taken through to the Boc-protected aminodiol **118**. Selective sulfonylation of the primary alcohol gave the mesitylenesulfonate **119** and treatment with base converted this into the epoxide **120**. This was converted into the pipecolic acid derivative **121** using trifluoroacetic acid that promoted cleavage of the *tert*-butoxycarbonyl group and cyclisation. The structure of the final product was assigned on the basis of the ^{1}H NMR data. These were more consistent with the pipecolic acid structure shown than the alternative seven-membered ring containing isomer. In particular the diastereotopic exocyclic methylene hydrogens were observed as sharp double-doublets at δ3.44 and δ3.61, and H(2) was a doublet of doublets at δ3.34 with axial-axial and axial-equatorial coupling constants of 10.8 and 2.6 Hz.

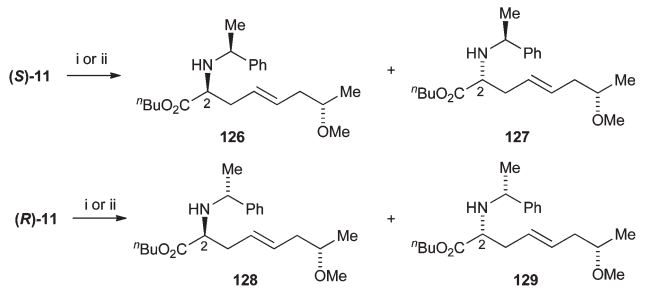
(*E*)-1,6-Stereocontrol in reactions between 5-hydroxy- and 5-methoxyhex-2-enylstannanes (*S*)-122 and (*S*)-123 with imines

Transmetalation of the 5-hydroxy- and 5-methoxyhex-2-enyl(tributyl)stannanes (***R*)-122** and (***R*)-123** using tin(IV) bromide generates allyltin tribromides that react with aldehydes with useful levels of 1,6-stereocontrol to give the (*Z*)-1,6-*syn*-alk-3-enols **124** and **125**.[8] Better results were obtained using tin(IV) bromide rather than tin(IV) chloride in these reactions. It was therefore

decided to investigate the stereoselectivity of reactions of the hex-2-enylstannanes **122** and **123** with imines.



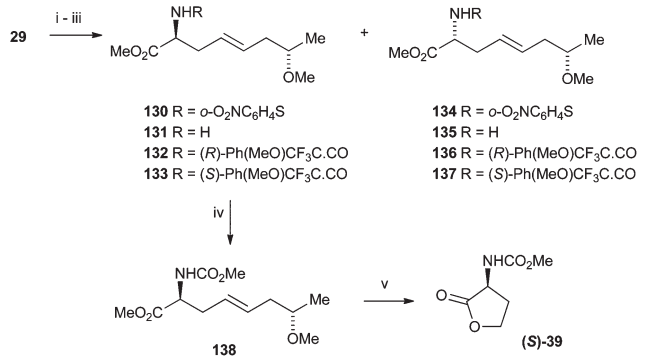
For the tin(IV) bromide promoted reactions between the chiral imines (***S*)-11** and (***R*)-11** and the (*S*)-5-methoxyhex-2-enylstannane (***S*)-123**, the major products **127** and **128** had the *unlike* configuration at C(2) relative to the stereogenic centre derived from the imine as shown by the H(2) chemical shifts of the *like*- and *unlike*-1,3-stereoisomers. It would appear that the stereoselectivities of these reactions are controlled primarily by the imine and not by the intermediate allyltin tribromide, see Scheme 16. Similar results were obtained using tin(IV) chloride although the yields were slightly lower.



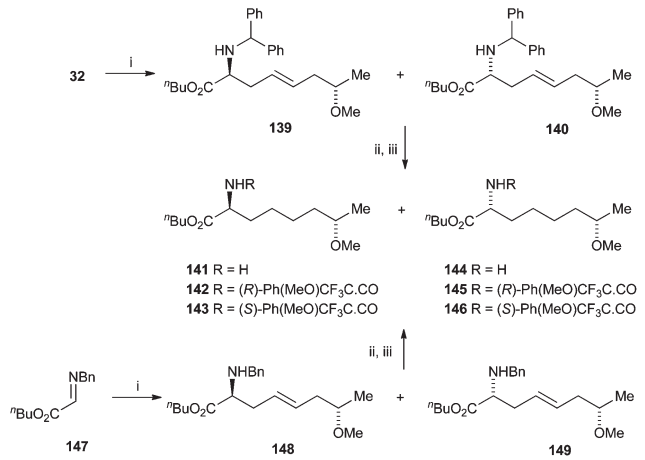
Scheme 16 Reactions between the 5-methoxyhex-2-enylstannane (***S*)-123** and chiral imines. Reagents and conditions: (i) (***S*)-123**, 78 °C, $SnBr_4$, 15 min, add imine, −50 °C, 8 h, then satd. aq. NH_4Cl (**126**/**127**, 68%; **126** : **127** = 16 : 84; **128**/**129**, 72%; **128** : **129** = 92 : 8); (ii) (***S*)-123**, 78 °C, $SnCl_4$, 15 min, add imine, −50 °C, 8 h, then satd. aq. NH_4Cl (**126**/**127**, 46%; **126** : **127** = 13 : 87; **128**/**129**, 58%; **128** : **129** = 75 : 25).

The tin(IV) bromide promoted reaction between the 5-methoxyhex-2-enylstannane (***S*)-123** and the achiral imine **29** gave a mixture of epimeric 2-amino-oct-4-enoates **130** and **134** see Scheme 17. These sulfanylamines could not be separated. On treatment with aqueous hydrogen chloride in methanol, they were cleaved to give a mixture of the corresponding amines **131** and **135**. This mixture was esterified with (*S*)- and (*R*)-Mosher's acid chlorides to give the separable Mosher's derivatives **132**/**136** and **133**/**137**. From the ratio of these derivatives it was estimated that the initial product mixture from the allylstannane contained the epimeric products in a 70 : 30 ratio. To establish the C(2) configuration of the major product, the mixture of amines **131** and **135** was converted into the carbamate **138** and ozonolysis with a reductive work-up and lactonisation of the hydroxyl ester so obtained gave the lactone (***S*)-39** identified by comparison with an authentic sample.[14] The major product from the allyltin reaction was therefore identified as the (2*S*)-epimer **130** with a reaction selectivity of *ca.* 70 : 30. The shielding effects of the phenyl group in the Mosher's derivatives were consistent with this assignment.[22]

The tin(IV) bromide promoted reactions between the (*S*)-5-methoxyhexenylstannane (***S*)-123** and the achiral *N*-benzyhydryl



Scheme 17 Tin(IV) bromide promoted reaction of stannane (***S*)-123** and imine **29**. Reagents and conditions: (i) (***S*)-123**, 78 °C, $SnBr_4$, 15 min, add imine, −50 °C, 9 h, then satd. aq. NH_4Cl (**130**/**134**, 58%; **130** : **134** = 70 : 30); (ii) HCl, MeOH, MeOH, r.t., 2 h (**131**/**135**, 92%); (iii) (*S*)- or (*R*)-Mosher's acid chloride, Et_3N, DMAP, CH_2Cl_2, r.t., 15 h (**132**/**136**, 74%, **132** : **136** = 70 : 30; **133**/**137**, 77%, **133** : **137** = 70 : 30); (iv) MeOC(O)Cl, K_2CO_3, $CHCl_3$, r.t., 16 h [**138** plus *ca.* 25% C(2)-epimer, 83%]; (v) (a) O_3, MeOH, 90 min., Me_2S, r.t., 90 min (b) $NaBH_4$, MeOH, 0 °C–r.t., 1 h (c) glacial HOAc, $CHCl_3$, heat under reflux, 16 h (58%; *ca.* 60% e.e.).

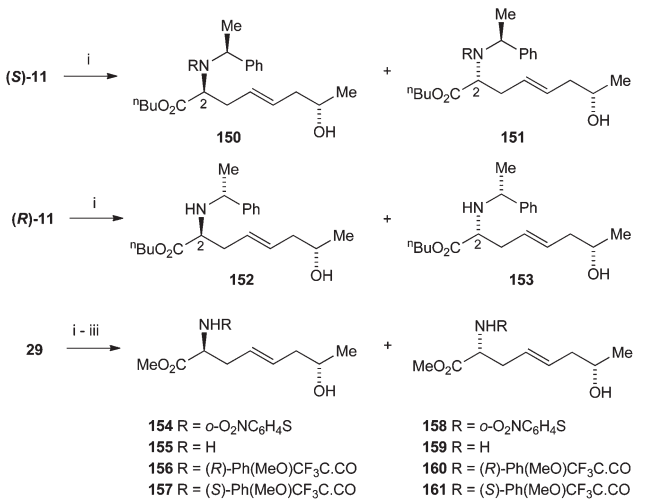


Scheme 18 Tin(IV) bromide promoted reactions of the stannane (***S*)-123** and imines **32** and **147**. Reagents and conditions: (i) (***S*)-123**, 78 °C, $SnBr_4$, 15 min, add imine, −45 °C or −50 °C, 22–24 h, then satd. aq. NH_4Cl (**139**/**140**, 62%; **139** : **140** = 70 : 30; **148**/**149**, 57%; **148** : **149** = 70 : 30); (ii) 10% Pd–C, ammonium formate, MeOH, r.t., 1 h (**141**/**144**, 92% from **139**/**140**; 96% from **148**/**149**); (iii) (*S*)- or (*R*)-Mosher's acid chloride, Et_3N, DMAP, CH_2Cl_2, r.t., 15 h (**142**/**145**, 76%, **142** : **145** = 70 : 30 from **139**/**140**; **143**/**146**, 75%, **143** : **146** = 70 : 30 from **139**/**140**; **142**/**145**, 77%, **142** : **145** = 70 : 30 from **148**/**149**; **143**/**146**, 71%, **143** : **146** = 70 : 30 from **148**/**149**).

and *N*-benzyl imines **32** and **147** were also investigated. Transfer hydrogenation of the mixtures of products that were obtained in each case effected debenzylation and double-bond hydrogenation. Mosher & Dale's derivatisation of the hydrogenolysis products allowed an estimate of the stereoselectivities of the original reactions and a comparison of the ^1H NMR spectra of the Mosher's derivatives was used to assign configurations to the products at C(2).[22] The *N*-benzyhydryl and *N*-benzylimines were thus shown to react with the allyltin tribromide generated from

the (*S*)-5-methoxy-hex-2-enylstannane (***S*)-120** with *ca.* 70 : 30 stereoselectivities in favour of the (2*S*)-epimers **139** and **148**, see Scheme 18.

Tin(IV) bromide promoted reactions of the (*S*)-5-hydroxyhex-2-enylstannane (***S*)-122** with the chiral imines (***S*)-11** and (***R*)-11** and with the achiral sulfenimine **29** gave similar results to those obtained for the 5-methoxyhexenylstannane (***S*)-123**. The reactions of the chiral imines were dominated by their preference for formation of the 1,3-*unlike* epimers **151** and **152** and the achiral imine **29** reacted with a preference for formation of the (*E*)-2,7-*anti*-diastereoisomer **154**. Structures were assigned to the products from the chiral imines (***S*)-11** and (***R*)-11** using the relative chemical shifts of H(2). The epimeric products from the achiral imine **29** could not be distinguished by NMR. The ratio of 86 : 14 was estimated from the ratios of the diastereoisomeric Mosher's derivatives **156**/**160** and **157**/**161** that were also used to assign the C(2) configuration of the major product **154**,[22] see Scheme 19.



Scheme 19 Reactions of the 5-hydroxyhexenylstannane (***S*)-122** with imines. Reagents and conditions: (i) (***S*)-122**, 78 °C, $SnBr_4$, 15 min, add imine, −45 °C, 24 h, then satd. aq. NH_4Cl (**150**/**151**, 69%; **150** : **151** = 13 : 87; **152**/**153**, 55%; **152** : **153** = 74 : 26; **154**/**158**, 60%; **154** : **158** = 86 : 14); (ii) HCl, MeOH, MeOH, r.t., 2 h (**155**/**159**, 97%); (iii) (*S*)- or (*R*)-Mosher's acid chloride, Et_3N, DMAP, CH_2Cl_2, r.t., 15 h (**156**/**160**, 69%, **156** : **160** = 86 : 14; **157**/**161**, 64%, **157** : **161** = 86 : 14).

There would appear to be a modest preference for formation of the (*E*)-2,7-*anti*-diastereoisomers **130**, **139**, **148** and **154** in the tin(IV) bromide promoted reactions between the 5-methoxy- and 5-hydroxy-hex-2-enylstannanes (***S*)-123** and (***S*)-122** with the achiral imines **29**, **32** and **147** although the stereoselectivities of the analogous reactions with the chiral imines (***S*)-11** and (***R*)-11** were dominated by the preference of the imine. The formation of the (*E*)-2,7-*anti*-isomers from the achiral imines is consistent with participation of the allyltin tribromide **162** that reacts with the imines *via* the chair-like transition structure **163** (or *via* an alternative open-chain process), see Fig. 7. Participation of the allyltin tribromide **162** has been invoked to explain the stereoselectivities of reactions of stannanes **122** and **123** with aldehydes.[8]

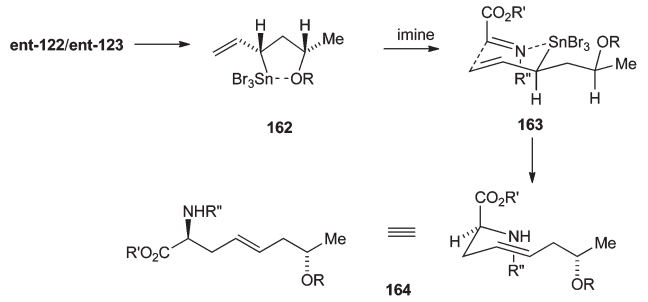
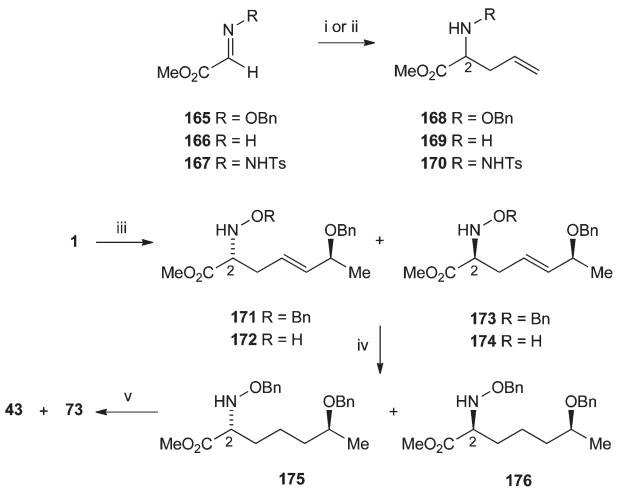


Fig. 7 Cyclic transition structure for the reaction of allyltin tribromides generated from the allylstannanes (***S*)-122** and (***S*)-123** with imines.



Scheme 20 Reactions between allyltin trichlorides and oximes or hydrazones. Reagents and conditions: (i) **3**, $SnCl_4$, −78 °C, 15 min, **165** or **166**, −78 °C, 4 h, then satd. aq. NH_4Cl (**168**, 82%, **169**, 80%); (ii) **3**, $SnCl_4$, −78 °C, 15 min, **167**, −45 °C, 50 h, then satd. aq. NH_4Cl (**170**, 61%); (iii) **1**, $SnCl_4$, 78 °C, 15 min, either **165** or **166**, −78 °C or −45 °C, 50 h, then satd. aq. NH_4Cl (**171**/**173**, 67%; **171** : **173** = 85 : 15; **172**/**174**, 64%; **172** : **174** = 87 : 13); (iv) $TsNHNH_2$, NaOAc, DME, heat under reflux, 2 h (96%; **175** : **176** = 85 : 15); (v) (a) HCO_2H, MeOH, 10% Pd/C, r.t., 16 h (b) Ac_2O, Et_3N, DMAP, CH_2Cl_2, r.t., 16 h (88%; **43** : **73** = 90 : 10).

1,5-Stereocontrol in reactions between the 4-benzyloxypent-2-enylstannane 1 and oximes

Preliminary studies were carried out on reactions between allyltin trichlorides with oximes and a hydrazone, see Scheme 20. The reactions of prop-2-enyltin trichloride with the oximes **165** and **166** were complete after 4 h at −78 °C; the hydrazone **167** was less reactive requiring 50 h at −45 °C for completion. The reactions of the oximes **165** and **166** with the 4-benzyloxypent-2-enylstannane **1** also required 50 h at −45 °C and at −78 °C, respectively, for completion. Nevertheless, these were stereoselective, giving mixtures of the (*E*)-2,6-*anti*- and (*E*)-2,6-*syn*-products in which the (*E*)-2,6-*anti*-epimers **171** and **172** were preferred, 2,6-*anti* : 2,6-*syn* = *ca.* 85 : 15. The structure of the major epimer from the reaction with the *O*-benzyloxime **165** was shown to correspond to the 2,6-*anti*-isomer **171** by reduction of the mixture of products **171** and **173** to give the heptanoates **175** and **176** followed by hydrogenolysis and acetylation. The major

2-acetamido-6-acetoxyheptanoate so obtained was found to correspond to the 2,6-*anti*-epimer **43** that had been prepared earlier. The products **172** and **174** from the reaction of the allyltin trichloride derived from the allylstannane **1** and the oxime **166** were unstable to storage. In this case, the major product was assigned the 2,6-*anti*-configuration by analogy with the selective formation of the 2,6-*anti*-epimer **171**, see Scheme 20.

Summary and conclusions

It has been shown that tin(IV) chloride promoted reactions of the 4-alkoxypent-2-enylstannane **1** with 1-alkoxycarbonylimines proceed with useful stereocontrol, typically greater than 90 : 10, in favour of (4*E*)-2,6-*anti*-2-alkylamino-6-alkoxyheptenoates **49**. This stereoselectivity overwhelmed the intrinsic diastereofacial preferences of *N*-α-methylbenzylimines. Analogous reactions of the 5-benzyloxy-4-methylpent-2-enylstannane **80** showed more enhanced matching and mismatching with the chiral imines but nevertheless showed useful 1,5-stereocontrol in reactions with achiral 1-alkoxycarbonylimines. The 4-alkoxy-5-silyloxypent-2-enylstannane **106** was also found to react with 1-alkoxycarbonylimines with excellent stereocontrol in favour of the (4*E*)-2,6-*anti*-2-alkylamino-6-alkoxyheptenoates **179**. The use of (*tert*-butyldimethylsilyloxy) substituted pent-2-enylstannanes in these reactions demonstrated complementary effects in that in the 4-alkoxy series the 1,5-stereoselectivity was reversed to give the 2,6-*syn*-diastereoisomers **79** albeit with lower overall stereoselectivity, whereas it was just slightly reduced in the 5-alkoxy series. Tin(IV) bromide promoted reactions of the 5-hydroxy- and 5-methoxyhex-2-enylstannanes (***S*)-122** and (***S*)-123** with achiral imines showed some 1,6-stereocontrol in favour of (4*E*)-2,7-*anti*-epimers, but the stereoselectivities of reactions with chiral imines were dominated by the stereochemical preferences of the imines. These results are summarised in Fig. 8.

The stereoselectivities of these reactions are consistent with stereoselective transmetalation of the alk-2-enylstannanes to generate the allyltin trihalides that had been postulated previously to explain remote stereocontrol in analogous reactions with aldehydes.[8,9] However, aldehydes give rise to the formation of (*Z*)-alkenes whereas (*E*)-alkenes were obtained for reactions with imines. This reversal in stereoselectivity is consistent with either six-membered cyclic or open-chain transition structures for the reactions of the intermediate allyltin trihalides with imines, *cf.* Fig. 3. However, since imines with electron withdrawing substituents were found to be the more reactive towards allyltin trihalides, that themselves are electron deficient reagents, it may be that the cyclic transition structures in which the imine is activated by co-ordination to the tin are involved, see Fig. 3–7. If this is the case, the preference for (*E*)-alkene formation may be due to the unfavourable 1,3-diaxial interactions between the group next to tin and the substituent on the nitrogen of the imine that would be present in the analogous transition structures for (*Z*)-alkene formation.[8,9,15,16]

The reactions of allyltin trihalides with imines tend to be slower than the analogous reactions with aldehydes. As epimeric allyltin trihalides can epimerise at the stereogenic centre next to the tin,[15] this may account for the reduced stereoselectivities observed for the reactions of the 5-alkoxystannanes with mis-

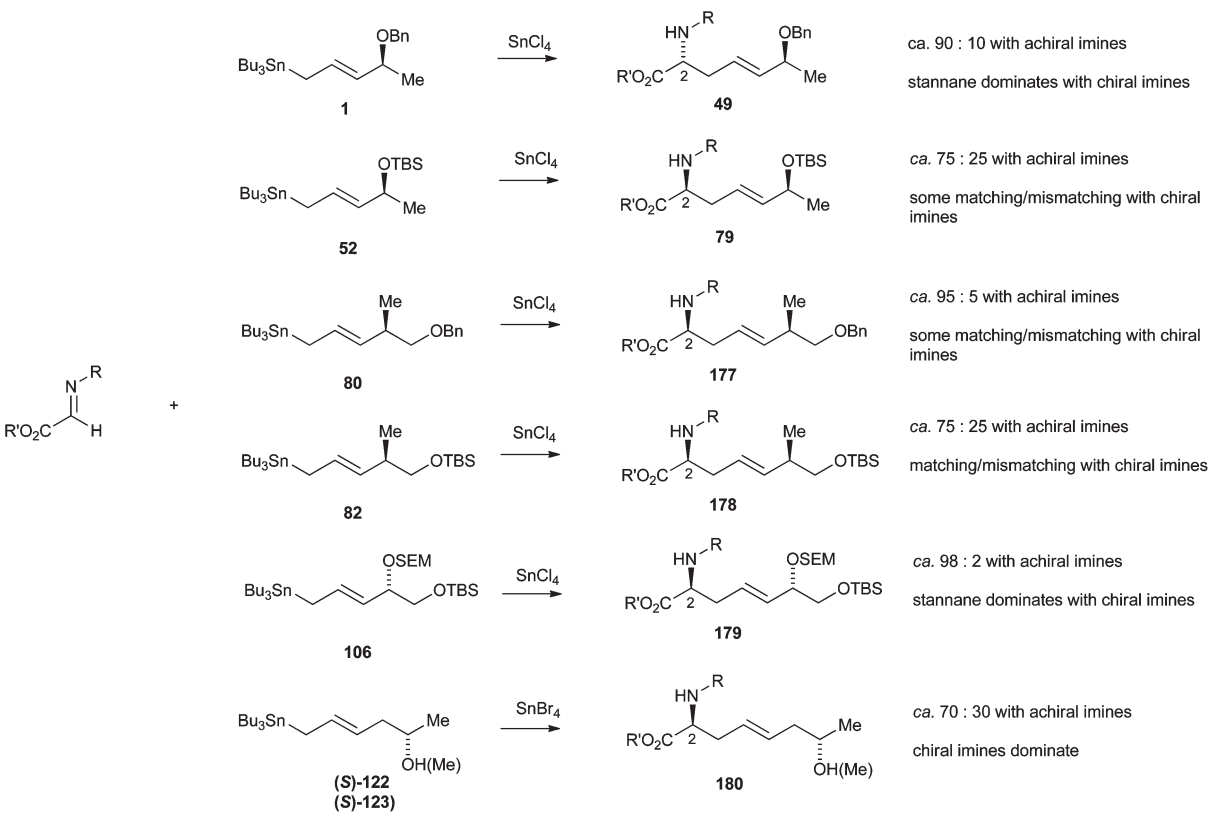


Fig. 8 Summary of remote stereoselectivities of reactions between imines and alkoxy- and hydroxy-stannanes.

matched chiral imines. Nevertheless for alk-2-enylstannanes with alkoxy substituents leading to 1,5-stereocontrol, stereoselectivities in excess of 90 : 10 were observed with achiral imines and this chemistry should be synthetically useful for the synthesis of novel α-amino acids.

Experimental

General experimental procedures

NMR spectra were obtained using Varian Unity 500, Bruker AC 300, or Varian XL 300 spectrometers. Chemical shifts are quoted in parts per million downfield from tetramethylsilane. Low resolution MS were obtained on a Fisons VG Trio 2000 spectrometer, using electron impact (EI) and chemical ionisation (CI) modes. Fast atom bombardment (FAB) and high resolution mass measurements were acquired on a Kratos Concept spectrometer. IR spectra were measured on an ATI Mattson Genesis Series FTIR spectrometer as evaporated thin films on sodium chloride plates. Optical rotations were measured at 589 nm at ambient temperature using an Optical Activity AA-100 polarimeter.

All non-aqueous reactions were performed in oven (140 °C) or flame-dried glassware under an inert atmosphere of dry nitrogen or argon. Solvents were dried immediately prior to use by distillation under an atmosphere of dry nitrogen from sodium benzophenone ketyl (diethyl ether, tetrahydrofuran, hexane), calcium hydride (DCM, dimethyl sulfoxide) or anhydrous potassium hydroxide (triethylamine, diisopropylamine, pyridine). Analytical grade toluene and benzene were dried over sodium wire for 24 h prior to use. Methanol was dried over magnesium turnings and then distilled. Petrol refers to that fraction of light petroleum ether which boils between 40 and 60 °C and was redistilled prior to use. Butyllithium was supplied as a solution in hexanes and was titrated against anhydrous butanol in tetrahydrofuran using 2,2′-dipyridyl as indicator. Ether refers to diethyl ether whilst brine refers to saturated aqueous sodium chloride. Preparative column chromatography was carried out using Merck silica 9385 (230–400 ASTM mesh) or Merck silica gel 60H (40–63μ, 230–300 mesh). Analytical high performance liquid chromatography (HPLC) was carried out using a pump controlled Gilson assembly with a Dynamax 60Å silica column with (dimensions of 21.4 × 250 mm) and a guard column, monitoring at 254 nm using a Gilson 115 UV detector.

The imines were prepared following literature procedures;[7] for the (*S*)-imine (***S*)-11**, $[\alpha]_D$ −48 (*c* 1.1 in $CHCl_3$), −24.04 (neat) [lit.[7] −18.2 (neat)]; for the (*R*)-imine (***R*)-11**, $[\alpha]_D$ +46.3 (*c* 1.7 in $CHCl_3$), +25.9 (neat).

General procedure for the reaction of an alkoxyalk-2-enylstannane with an imine

The tin(IV) halide in DCM was cooled to −78 °C and the allylstannane (1.05 molar equivalents based on the amount of Lewis acid) in cooled (−78 °C) DCM was added. After fifteen minutes, the imine (1.05 molar equivalents based on the amount of Lewis acid) in DCM was added dropwise by syringe over five minutes whilst maintaining the reaction at −78 °C. The resulting solution or suspension was stirred at either −78 °C, −50 °C or −45 °C for the appropriate time. Saturated aqueous ammonium chloride was then added and the mixture stirred vigorously whilst being allowed to warm to ambient temperature. Water was added and the mixture extracted DCM. The aqueous phase was basified to pH 10 by the addition of aqueous sodium hydroxide (1 M) and washed with DCM. The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue gave the product.

In some cases, water (0.5 mL) was added to the reaction mixture and, after stirring to ambient temperature, silica was added (*ca*. 5 g). The solvent was then carefully removed under reduced pressure to afford a powder that was applied to a column of silica gel.

General procedure for the deprotection of nitrophenylsulfanylamines

The nitrophenylsulfanylamine was dissolved in the minimum volume of methanol and saturated methanolic hydrogen chloride (typically 10 mL for 1 mmol of substrate) added. The resulting yellow suspension was stirred at ambient temperature for 2 h before concentration under reduced pressure. The residue was suspended in chloroform and extracted twice with aqueous hydrogen chloride (1 M). The aqueous washings were basified by the addition of solid sodium hydrogen carbonate and the mixture extracted into ether. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure.

General procedure for the preparation of methyl carbamates

Anhydrous potassium carbonate (2 molar equivalents) and methyl chloroformate (2 molar equivalents) were added to the amine and the suspension stirred at ambient temperature for 16 h. Water was added and, after 10 min, the mixture was extracted with chloroform. The organic layer was dried ($MgSO_4$), absorbed on to silica and the resulting powder applied to a column of silica gel.

General procedure for the cbz-protection of α-amino esters

Anhydrous potassium carbonate (2 molar equivalents) and benzyl chloroformate (1.3 molar equivalents) were added to the α-amino ester in chloroform (typically 10 mL for a 1 mmol and the mixture was heated under reflux for 16 h. After cooling to ambient temperature, chloroform was added and the mixture washed with water and brine. The organic extracts were dried ($MgSO_4$), absorbed on to silica and the resulting powder was applied to a column of silica gel.

General procedure for the ozonolysis of unsaturated α-amido esters followed by reduction using $NaBH_4$ and lactonisation

The α-amido ester in methanol (typically 20 mL for 1 mmol of substrate) was cooled to −78 °C and ozone bubbled through the solution for 90 min at −78 °C (a permanent blue colour appeared after *ca.* twenty minutes depending on the scale). The mixture was purged with nitrogen, methyl sulfide (3 molar equivalents based on the cbz-derivative) was added as a single portion and the reaction mixture stirred whilst being allowed to warm to

ambient temperature over 1 h. After concentration under reduced pressure, the residue was dissolved in methanol and the solution was cooled to 0 °C.

Sodium borohydride (4 molar equivalents based on the substrate) was added and the reaction mixture stirred at ambient temperature for 30 min. Saturated aqueous ammonium chloride was added and the mixture concentrated under reduced pressure. The residue was suspended in DCM, and the mixture washed with water, aqueous hydrogen chloride (0.1 M) and water and then dried ($MgSO_4$). Concentration under reduced pressure gave the alcohol.

The alcohol was dissolved in the minimum volume of methanol, hydrochloric acid (37% w/v) was added (typically 5 mL for a 1 mmol reaction) and the reaction mixture stirred at ambient temperature for 16 h. The resulting suspension was poured into water and solid sodium hydrogen carbonate added until neutral. The methanol was removed under reduced pressure and the aqueous residue extracted twice with ethyl acetate. The organic extracts were washed with brine, dried ($MgSO_4$) and absorbed on to silica. The resulting powder was applied directly to a column of silica gel and elution with hexane–ethyl acetate (4 : 1) afforded the lactones.

Alternatively, the alcohol was dissolved in chloroform (*ca.* 10 mL for a 1 mmol reaction), glacial acetic acid (catalytic) was added and the solution heated under reflux for 16 h. After cooling to ambient temperature, the mixture was washed with a saturated aqueous sodium hydrogen carbonate, dried ($MgSO_4$) and absorbed on to silica. The ensuing powder was applied to a column of silica gel.

General procedure for the removal of the cbz-group from homoserine lactone derivatives

Ammonium formate (5 molar equivalents based on the lactone) and 10% Pd/C (10% w/w based on the lactone) were added to the cbz-protected lactone in methanol (typically 0.05 molar concentration) and the mixture stirred at ambient temperature for 30 min. The mixture was filtered (Whatman glass microfibre filter paper GF/A) and the solution absorbed on to silica. The resulting powder was applied to a small column of silica gel. Elution with chloroform–methanol–triethylamine (99 : 0.5 : 0.5) gave the amino lactone.

General procedure for the removal of benzyl and benzhydryl groups from α-amino esters

A solution of formic acid (98%) in methanol (10% v/v) was freshly prepared and the protected amino ester was dissolved in this solution typically at ~0.075 molar concentration. 10% Pd/C (15% w/w based on the ester) was added and the reaction mixture stirred at ambient temperature for 16 h. The mixture was filtered (Whatman glass microfibre filter paper GF/A) and the solution concentrated under reduced pressure to give an oil. Any remaining formic acid was removed by adding heptane to the residue and concentrating under a high vacuum (three times).

General procedures for the acylation of α-amino esters

The α-amino ester was dissolved in DCM (typically 10 mL for a 1 mmol reaction) and triethylamine (3 molar equivalents), acetic anhydride (1.5 molar equivalents) and DMAP (catalytic) were added. The mixture was stirred at ambient temperature for 16 h before water was added to the reaction mixture and the stirring continued for 10 min. DCM was added and the organic extract washed with a saturated aqueous sodium hydrogen carbonate and dried ($MgSO_4$). This solution was absorbed on to silica and the resulting powder applied to a column of silica gel.

Alternatively, the α-amino ester was dissolved in DCM (typically 10 mL for a 1 mmol reaction) and triethylamine (6 molar equivalents), acetic anhydride (3 molar equivalents) and DMAP (catalytic) were added. This mixture was stirred at ambient temperature for 16 h then worked up as above.

General procedure for the diimide reduction of alkenes

The alkene and toluene 4-sulfonylhydrazine (10 molar equivalents based on the alkene) in DME (typically 15 mL for a 1 mmol reaction) were heated under reflux. Anhydrous sodium acetate (10 molar equivalents based on the alkene) dissolved in the minimum volume of water was added over a period of two hours whilst maintaining the reaction under reflux. The heating was continued for a further 16 h and the reaction was then cooled to ambient temperature and concentrated under reduced pressure. The residue was suspended in ether and the mixture washed with saturated aqueous sodium hydrogen carbonate and water then dried ($MgSO_4$). The solution was absorbed on to silica and the resulting powder applied to a column of silica gel.

Ethyl *N*-(1-phenylbut-3-en-1-yl)carbamate 9

The general procedure using tin(IV) chloride (261 mg, 1.00 mmol) in DCM (5 mL), prop-2-enyl(tributyl)stannane **3** (348 mg, 1.05 mmol) in DCM (5 mL) and imine **8** (186 mg, 1.05 mmol) after 4 h at −78 °C with chromatography using hexane–ether–triethylamine (80 : 19.5 : 0.5) as eluent gave the *title compound* **9** (201 mg, 92%) as a colourless liquid (Found: $M^+ + NH_4$, 237.1596. $C_{13}H_{21}N_2O_2$ requires *M*, 237.1603); ν_{max}/cm^{-1} 701, 761, 918, 994, 1048, 1077, 1098, 1173, 1253, 1334, 1373, 1440, 1534, 1642, 1693, 2981 and 3324; δ_H (300 MHz, $CDCl_3$) 1.26 (3 H, *t*, *J* 7.1, CH_3), 2.56–2.60 (2 H, m, 2-CH_2), 4.13 (2 H, q, *J* 7.1, CH_3CH_2), 4.80 (1 H, m, 1-H), 5.09 (1 H, br s, NH), 5.12–5.19 (2 H, m, 4-H_2), 5.73 (1 H, m, 3-H) and 7.26–7.40 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 14.58, 41.14, 54.38, 60.91, 118.40, 126.24, 127.29, 128.57, 133.84, 142.18 and 155.94; *m*/*z* (CI) 237 (M^+ + 18, 100%) and 220 (M^+ + 1, 12).

Butyl (2*S*)- and (2*R*)-2-[(*R*)-(1-phenylethyl)amino]pent-4-enoate 12 and 13

The general procedure using tin(IV) chloride (12.48 g, 47.9 mmol) in DCM (40 mL), prop-2-enyl)tributyl)stannane **3** (16.66 g, 50.3 mmol) in DCM (40 mL) and the (*R*)-imine (***R*)-11** (11.74 g, 50.3 mmol) after 4 h at −78 °C with chromatography

using petrol–ether–triethylamine (90 : 9.5 : 0.5) as eluent gave the *title compounds* **12** and **13** (11.87 g, 90%) as a colourless liquid, ratio **12** : **13** = 93 : 7 (^{1}H NMR). Samples of each isomer were obtained by preparative scale HPLC (Rainin Dynamax silica column, UV at 254 nm, eluent hexane–ethyl acetate 6 : 1, flow rate 15 mL min^{-1}): the less polar minor (2*R*)-pent-4-enoate **13**[7] (Found: M^+ + H, 276.1959. $C_{17}H_{26}NO_2$ requires M, 276.1964); $[\alpha]_D$ +33 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 771, 921, 1151, 1186, 1218, 1454, 1646, 1732, 2963 and 3331; δ_H (500 MHz, $CDCl_3$) 0.91 (3 H, t, *J* 7.3, CH_3CH_2), 1.30–1.38 (2 H, m, CH_3CH_2), 1.31 (3 H, d, *J* 6.4, $CHCH_3$), 1.58 (2 H, qn, *J* 6.6, CH_2CH_2O), 1.90 (1 H, br s, NH), 2.29–2.32 (2 H, m, 3-H_2), 3.07 (1 H, t, *J* 6.4, 2-H), 3.69 (1H, q, *J* 6.4, $CHCH_3$), 4.10 (2 H, t, *J* 6.6, CH_2O), 5.01–5.06 (2 H, m, 5-H_2), 5.68 (1 H, m, 4-H) and 7.27–7.31 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 13.69, 19.15, 25.34, 30.75, 38.27, 56.60, 58.61, 64.40, 117.74, 126.92, 127.06, 128.40, 133.84, 145.01 and 175.31; *m*/*z* (CI) 276 (M^+ + 1, 100%); the more polar major (2*S*)-pent-4-enoate **12** (Found: C, 74.1; H, 9.5; N, 5.0. $C_{17}H_{25}NO_2$ requires C, 74.1; H, 9.2; N, 5.1); $[\alpha]_D$ +23.2 (*c* 0.6 in $CHCl_3$); ν_{max}/cm^{-1} 762, 917, 967, 996, 1026, 1064, 1183, 1273, 1342, 1372, 1453, 1493, 1603, 1641, 1734, 2961 and 3330; δ_H (500 MHz, $CDCl_3$) 0.89 (3 H, t, *J* 7.5, CH_3CH_2), 1.28–1.35 (2 H, m, CH_3CH_2), 1.32 (3 H, d, *J* 6.6, $CHCH_3$), 1.53 (2 H, qn, *J* 7.1, CH_2CH_2O), 1.86 (1 H, br s, NH), 2.37–2.40 (2 H, m, 3-H_2), 3.35 (1 H, t, *J* 6.3, 2-H), 3.76 (1H, q, *J* 6.6, $CHCH_3$), 3.93–4.02 (2 H, m, CH_2O), 5.02–5.10 (2 H, m, 5-H_2), 5.74 (1 H, m, 4-H) and 7.27–7.32 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 13.78, 19.21, 23.22, 30.69, 37.52, 56.09, 58.70, 64.45, 117.80, 126.66, 127.00, 128.28, 133.55, 145.02 and 174.33; *m*/*z* (CI) 276 (M^+ + 1, 100%).

Potassium *tert*-butoxide in THF (1 M; 11 mL) was added to the (*S*)-ester **12** (2.76 g, 10 mmol) in cooled (−78 °C) THF (30 mL) over a period of five minutes with and the mixture stirred at −78 °C for ten minutes. Water (10 mL) was added and mixture stirred vigorously whilst warming to ambient temperature. After concentration under reduced pressure, the residue dissolved in ether and the solution washed with water, brine, dried ($MgSO_4$) and absorbed on to silica. The resulting powder was applied to a column of silica gel and elution with hexane–ether–triethylamine (90 : 9.5 : 0.5) gave the esters **12** and **13** (2.43 g, 88%) in the ratio 17 : 83 (^{1}H NMR). Preparative scale HPLC gave the (2*R*)-isomer **13** (1.67 g) together with the (2*S*)-isomer **12** (346 mg) as colourless oils.

Following the general procedure, tin(IV) chloride (1.13 g, 4.34 mmol) in DCM (7 mL), prop-2-enyl(tributyl)stannane **3** (1.51 g, 4.56 mmol) in DCM (7 mL) and the (*S*)-imine (***S*****)-11** (1.07 g, 4.57 mmol) after chromatography using petrol–ether–triethylamine (90 : 9.5 : 0.5) as eluent, gave butyl (2*R*)- and (2*S*)-2-[(*S*)-(1-phenylethyl)amino]-pent-4-enoate ***ent*-12** and ***ent*-13** (1.05 g, 88%) as a colourless liquid, ***ent*-12** : ***ent*-13** = 93 : 7 (^{1}H NMR). Further chromatography gave the (2*R*)-isomer ***ent*-12**, $[\alpha]_D$ −23 (*c* 1.0 in $CHCl_3$). Spectroscopic data were identical to those of the enantiomer **12**.

Butyl (2*R*)-2-{(2,2,2-trichloro-1,1-dimethylethoxy)carbonyl-[(*S*)-(1-phenylethyl)]amino}pent-4-enoate 14

Anhydrous potassium carbonate (1.0 g), (2,2,2-trichloro-1,1-dimethyl)ethyl chloroformate (1.0 g, 4.17 mmol) was added to the α-amino ester ***ent*-12** (1.0 g, 3.64 mmol) in 1,4-dioxane (20 mL) and the mixture was heated under reflux for 16 h. After cooling to ambient temperature and concentration under reduced pressure, the residue was suspended in ether (60 mL). The solution was washed with water and brine, dried ($MgSO_4$) and absorbed on to silica. The resulting powder was applied to a column of silica gel to give the *title compound* **14** (1.57 g, 90%) as a colourless oil that crystallised on standing as colourless prisms, m.p. 71–72 °C; $[\alpha]_D$ −24.7 (*c* 1.2 in CH_2Cl_2); ν_{max}/cm^{-1} 701, 798, 848, 892, 916, 994, 1027, 1074, 1166, 1319, 1369, 1385, 1420, 1454, 1497, 1642, 1706, 1740 and 2960; δ_H (300 MHz, $CDCl_3$) 0.97 (3 H, t, *J* 7.3, CH_3CH_2), 1.44 (2 H, hex, *J* 7.5, CH_3CH_2), 1.56–1.69 (2 H, m, CH_2CH_2O), 1.62 (3 H, d, *J* 7.2, $CHCH_3$), 1.99 and 2.04 (each 3 H, s, CH_3), 2.31 (0.4 H, m, 3-H, minor rotamer), 2.73 (1 H, m, 3-H), 2.86 (0.6 H, m, 3-H, major rotamer), 3.49 (0.6 H, dd, *J* 8.1 and 5.1, 2-H, major rotamer), 4.01–4.24 (2.4 H, m, CH_2O and 2-H, minor rotamer), 4.56 (1 H, m, 5-H), 4.68 (1 H, m, 5-H), 5.08 (0.4 H, m, 4-H, minor rotamer), 5.26 (0.6 H, m, 4-H, major rotamer), 5.66 (1H, m, PhCH) and 7.34–7.39 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$, major rotamer) 13.72, 16.57, 19.27, 21.56, 21.66, 30.66, 35.18, 55.04, 56.70, 65.02, 88.95, 116.58, 128.07, 128.46, 135.32, 139.72, 148.54, 152.44 and 171.34; *m*/*z* (CI) 480 (M^+ + 1, 10%), 478 (M^+ + 1, 10) and 276 (100).

The enantiomeric carbamate ***ent*-14** was similarly prepared (Found: C, 55.1; H, 6.4; N, 2.9. $C_{22}H_{30}Cl_3NO_4$ requires C, 55.2; H, 6.3; N, 2.9); $[\alpha]_D$ +23 (*c* 1.04 in CH_2Cl_2). Spectroscopic data were identical to those of the enantiomer **14**.

Butyl (2*R*,6*S*,*E*)- and (2*S*,6*S*,*E*)-6-benzyloxy-2-[(*S*)-(1-phenylethyl)amino]hept-4-enoate 15 and 16

The general procedure using tin(IV) chloride (651 mg, 2.50 mmol) in DCM (8 mL), the 4-benzyloxypent-2-enylstannane **1** (1.22 g, 2.62 mmol) in DCM (8 mL) and the imine (***S*****)-11** (612 mg, 2.62 mmol) in DCM (8 mL) after 12 h at −45 °C and chromatography using petrol–ether–triethylamine (90 : 9.5 : 0.5) as eluent gave the *title compounds* **15** and **16** (747 mg, 73%) as a colourless oil, ratio **15** : **16** = 96 : 4 (^{1}H NMR). Further chromatography using petrol–ether (9 : 1) as the eluent gave a sample of the major (2*R*)-epimer **15** as a colourless oil (Found: M^+ + H, 410.2690. $C_{26}H_{36}NO_3$ requires *M*, 410.2695); $[\alpha]_D$ −26 (*c* 1.6 in $CHCl_3$); ν_{max}/cm^{-1} 700, 736, 972, 1028, 1071, 1153, 1182, 1275, 1372, 1453, 1494, 1732, 2870, 2963 and 3360; δ_H (300 MHz, $CDCl_3$) 0.95 (3 H, t, *J* 7.3, CH_3CH_2), 1.30 (3 H, d, *J* 6.5, 7-H_3), 1.34–1.44 (2 H, m, CH_3CH_2), 1.39 (3 H, d, *J* 6.5, $CHCH_3$), 1.60 (2 H, qn, *J* 7.4, CH_2CH_2O), 1.94 (1 H, br s, NH), 2.35–2.51 (2 H, m, 3-H_2), 3.43 (1 H, t, *J* 6.1, 2-H), 3.84 (1 H, q, *J* 6.5, PhC*H*), 3.92 (1 H, qn, *J* 6.8, 6-H), 4.04 (2 H, t, *J* 6.7, CH_2CH_2O), 4.38 and 4.57 (each 1 H, d, *J* 11.9, PhHC*H*O), 5.53 (1 H, dd, *J* 15.5 and 7.5, 5-H), 5.63 (1 H, dt, *J* 15.5 and 6.7, 4-H) and 7.24–7.38 (10 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 13.70, 19.15, 21.71, 23.21, 30.66, 35.93, 56.10, 58.85, 64.55, 69.73, 75.47, 126.75, 127.17, 127.39, 127.69, 128.34, 128.46, 135.53, 138.85, 145.23 and 174.46; *m*/*z* (CI) 410 (M^+ + 1, 100%). Minor peaks in the mixture of epimers were attributed to the (2*S*)-epimer **16**; δ_H (300 MHz, $CDCl_3$) 3.13 (t, *J* 6.1, 2-H).

Butyl (2*R*,6*S*,*E*)- and (2*S*,6*S*,*E*)-6-benzyloxy-2-[(*R*)-(1-phenylethyl)amino]hept-4-enoate 17 and 18

The general procedure using tin(IV) chloride (782 mg, 3.00 mmol) in DCM (9 mL), the 4-benzyloxypent-2-enylstannane **1** (1.47 g, 3.16 mmol) in DCM (9 mL) and the imine (*R*)-**11** (735 mg, 3.15 mmol) in DCM (9 mL) after 12 h at −45 °C and chromatography using petrol–ether–triethylamine (90 : 9.5 : 0.5) as eluent gave the *title compounds* **17** and **18** (884 mg, 72%) as a colourless oil, ratio **17** : **18** = 92 : 8 (^{1}H NMR). Further chromatography using petrol–ether (9 : 1) as the eluent gave a sample of the major (2*R*)-epimer **17** as a colourless oil (Found: M^+ + H, 410.2692. $C_{26}H_{36}NO_3$ requires *M*, 410.2695); $[\alpha]_D$ +33 (*c* 1.4 in $CHCl_3$); ν_{max}/cm^{-1} 699, 736, 972, 1029, 1071, 1153, 1180, 1372, 1454, 1495, 1733, 2870, 2963 and 3334; δ_H (300 MHz, $CDCl_3$) 0.98 (3 H, t, *J* 7.3, C*H*$_3$CH$_2$), 1.30 (3 H, d, *J* 6.4, 7-H$_3$), 1.34–1.45 (2 H, m, CH$_3$C*H*$_2$), 1.37 (3 H, d, *J* 6.5, CHC*H*$_3$), 1.64 (2 H, qn, *J* 7.3, C*H*$_2$CH$_2$O), 1.85 (1 H, br s, NH), 2.35–2.40 (2 H, m, 3-H$_2$), 3.14 (1 H, t, *J* 6.7, 2-H), 3.76 (1 H, q, *J* 6.5, PhCH), 3.91 (1 H, qn, *J* 6.8, 6-H), 4.10–4.24 (2 H, m, CH$_2$C*H*$_2$O), 4.37 and 4.54 (each 1 H, d, *J* 11.9, PhHC*H*O), 5.49 (1 H, dd, *J* 15.5 and 7.4, 5-H), 5.60 (1 H, dt, *J* 15.5 and 6.7, 4-H) and 7.30–7.36 (10 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 13.69, 19.16, 21.65, 25.34, 30.77, 36.75, 56.68, 58.93, 64.48, 69.78, 75.55, 126.93, 127.38, 127.69, 127.85, 128.34, 128.40, 135.27, 138.90, 145.01 and 175.2; *m*/*z* (CI) 410 (M^+ + 1, 100%). Minor peaks in the mixture of epimers were attributed to the (2*S*)-epimer **18**; δ_H (300 MHz, $CDCl_3$) 2.43–2.50 (m, 3-H$_2$), 3.43 (t, *J* 6.7, 2-H), 4.04 (t, *J* 6.7, CH$_2$C*H*$_2$O).

Butyl (2*S*)-2-{benzyloxycarbonyl-[(*R*)-(1-phenyl)ethyl]amino}-pent-4-enoate 19

The general procedure using amino ester **12** (1.80 g, 6.54 mmol), anhydrous potassium carbonate (1.81 g, 13.10 mmol) and benzyl chloroformate (1.20 mL, 8.51 mmol) after chromatography using hexane–ether (98 : 2 to 9 : 1) gave the *title compound* **19** (2.44 g, 91%) as a colourless oil (Found: C, 73.2; H, 7.7; N, 3.7. $C_{25}H_{31}NO_4$ requires C, 73.3; H, 7.6; N, 3.4); $[\alpha]_D$ +32.5 (*c* 0.6 in $CHCl_3$); ν_{max}/cm^{-1} 700, 741, 769, 916, 996, 1028, 1043, 1075, 1135, 1209, 1261, 1310, 1380, 1428, 1497, 1701, 1741 and 2960; δ_H (400 MHz, toluene-d$_8$, 90 °C) 0.79 (3 H, t, *J* 7.3, C*H*$_3$CH$_2$), 1.21 (2 H, hex, *J* 7.4, CH$_3$C*H*$_2$), 1.39 (2 H, qn, *J* 7.1, C*H*$_2$CH$_2$O), 1.51 (3 H, d, *J* 6.6, CHC*H*$_3$, major rotamer), 1.61 (3 H, d, *J* 7.0, CHC*H*$_3$, minor rotamer), 2.16 (1 H, m, 3-H), 2.88 (1 H, m, 3-H), 3.63 (1 H, dd, *J* 7.8 and 5.6, 2-H), 3.86–4.02 (2 H, m, CH$_2$C*H*$_2$O), 4.57–4.71 (2 H, m, 5-H$_2$), 5.07 and 5.13 (each 1 H, d, *J* 12.4, PhHC*H*O), 5.43 (1 H, m, 4-H), 5.56 (1 H, q, *J* 6.6, PhCH) and 7.00–7.26 (10 H, m, ArH); *m*/*z* (CI) 410 (M^+ + 1, 30%) and 276 (100).

(3*S*)-3-{*N*-Benzyloxycarbonyl-[(*R*)-1-(phenyl)ethyl]amino}-butyrolactone 21

The general procedure using the cbz-protected aminoester **19** (2.40 g, 5.86 mmol), ozone, methyl sulfide (1.29 mL, 17.57 mmol) and sodium borohydride (887 mg, 23.45 mmol) gave the alcohol **20** that was cyclised using hydrogen chloride in methanol to afford the *title compound* **21** (1.57 g, 79%) as a white powder. A single recrystallisation from DCM–hexane gave the lactone **21** as colourless needles, m.p. 151–153 °C (Found: C, 70.6; H, 6.3; N, 4.3. $C_{20}H_{21}NO_4$ requires C, 70.8; H, 6.25; N, 4.15); $[\alpha]_D$ +21 (*c* 1.1 in $CHCl_3$); ν_{max}/cm^{-1} 699, 1027, 1139, 1180, 1210, 1277, 1310, 1426, 1450, 1696, 1779 and 2976; δ_H (300 MHz, $CDCl_3$, mixture of rotamers) 1.64–1.80 (1 H, m), 1.68 (3 H, d, *J* 7, CHC*H*$_3$), 2.21 (0.45 H, m, minor rotamer), 2.46 (0.55 H, m, major rotamer), 3.66 (1 H, m, 3-H), 3.90–4.12 (1.45 H, m, 5-H), 4.44 (0.55 H, m, 5-H, major rotamer), 5.11 (0.45 H, d, *J* 12, PhHC*H*, minor rotamer), 5.23–5.36 (1.55 H, m, PhHC*H*), 5.57 (0.55 H, m, C*H*CH$_3$ major rotamer), 5.73 (0.45 H, m, C*H*CH$_3$, minor rotamer) and 7.30–7.45 (10 H, m, ArH); δ_C (75 MHz, $CDCl_3$, both rotamers) 16.46, 17.15, 26.41, 27.37, 51.48, 52.51, 54.22, 54.33, 65.10, 65.56, 67.78, 68.28, 127.45, 127.67, 127.90, 127.95, 128.25, 128.37, 128.44, 128.61, 128.74, 135.55, 136.21, 140.11, 154.79, 154.99, 174.75 and 174.96; *m*/*z* 357 (M^+ + 18, 100%) and 340 (M^+ + 1, 15).

(3*S*)-3-[(*R*)-1-(phenyl)ethyl]aminobutyrolactone 22

The general procedure using lactone **21** (150 mg, 0.442 μmol), ammonium formate (139 mg, 2.20 mmol) and 10% Pd/C (15 mg) gave the *title compound* **22** (64 mg, 71%) as a colourless oil (Found: M^+ + 1, 206.1179. $C_{12}H_{16}NO_2$ requires *M*, 206.1181); $[\alpha]_D$ +29.6 (*c* 1.5 in $CHCl_3$); ν_{max}/cm^{-1} 1022, 1165, 1311, 1378, 1452, 1494, 1604, 1772, 2915 and 3326; δ_H (300 MHz, $CDCl_3$) 1.45 (3 H, d, *J* 6.7, CHC*H*$_3$), 2.06–2.20 (2 H, m, 4-H and NH), 2.45 (1 H, m, 4-H), 3.35 (1 H, dd, *J* 10.9 and 8.1, 3-H), 3.84 (1 H, q, *J* 6.7, C*H*CH$_3$), 4.10 (1 H, ddd, *J* 11.0, 9.3 and 6.0, 5-H), 4.36–4.43 (1 H, m, 5-H) and 7.28–7.42 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 24.43, 30.85, 53.91, 56.49, 65.67, 126.41, 127.46, 128.84, 143.90 and 177.62; *m*/*z* (CI) 206 (M^+ + 1, 100%).

Butyl (2*R*)-2-{benzyloxycarbonyl-[(*R*)-(1-phenyl)ethyl]amino}-pent-4-enoate 23

The general procedure using amine **13** (1.0 g, 3.63 mmol), anhydrous potassium carbonate (1.0 g, 7.24 mmol) and benzyl chloroformate (666 μL, 4.72 mmol) after chromatography using hexane–ether (98 : 2 to 9 : 1) as eluent gave the *title compound* **23** (1.40 g, 94%) as a colourless oil (Found: M^+ + Na, 432.2152. $C_{25}H_{31}NO_4Na$ requires *M*, 432.2151; $[\alpha]_D$ +38.2 (*c* 1.1 in $CHCl_3$); ν_{max}/cm^{-1} 699, 745, 910, 1028, 1140, 1208, 1309, 1428, 1453, 1703, 1733 and 2957; δ_H (300 MHz, $CDCl_3$, a mixture of rotamers) 0.88 (3 H, t, *J* 7.1, C*H*$_3$CH$_2$), 1.11–1.26 (2 H, m, CH$_3$C*H*$_2$), 1.27–1.40 (2 H, m, C*H*$_2$CH$_2$O), 1.60 (3 H, d, *J* 7.1, CHC*H*$_3$), 2.50–2.80 (1 H, m, 3-H), 2.90–3.10 (1 H, m, 3-H), 3.52–3.95 (3 H, m, 2-H and CH$_2$C*H*$_2$O), 5.10–5.35 (4 H, m, 5-H$_2$ and PhCH$_2$), 5.50–5.80 (1 H, m, 4-H), 5.90 (1 H, q, *J* 7.1, C*H*CH$_3$) and 7.25–7.49 (10 H, m, ArH); *m*/*z* (FAB) 432 (M^+ + 23, 2%), 410 (M^+ + 1, 40) and 276 (100).

(3*R*)-3-{*N*-Benzyloxycarbonyl-[(*R*)-1-(phenyl)ethyl]amino}-butyrolactone 25

The general procedure using the cbz-protected aminoester **23** (1.40 g, 3.42 mmol), ozone, methyl sulfide (753 μL,

10.25 mmol) and sodium borohydride (517 mg, 13.67 mmol) gave the alcohol **23** that was cyclised using hydrogen chloride in methanol to afford the *title compound* **25** (838 mg, 72%) as a white powder. A single recrystallisation from DCM–hexane gave the lactone **25** as colourless needles, m.p. 126–128 °C (Found: C, 70.5; H, 6.1; N, 4.3. $C_{20}H_{21}NO_4$ requires C, 70.8; H, 6.2; N, 4.1); $[\alpha]_D$ +43 (*c* 0.5 in $CHCl_3$); ν_{max}/cm^{-1} 699, 751, 1023, 1143, 1178, 1214, 1271, 1308, 1426, 1496, 1697, 1780 and 2977; δ_H (300 MHz, $CDCl_3$, mixture of rotamers) 1.54 (3 H, d, *J* 6.9, $CHCH_3$), 2.27–2.42 and 2.55–2.67 (each 1 H, m), 3.65 (1 H, t, *J* 9.5, 3-H), 3.95–4.15 (1.5 H, m, 5-H), and 4.45 (0.5 H, m, 5-H), 5.02–5.35 (2 H, m, $PhCH_2$), 5.50 and 5.69 (each 0.5 H, m, $CHCH_3$), 7.24–7.39 (8 H, m, ArH) and 7.46–7.52 (2 H, m, ArH); δ_C (75 MHz, $CDCl_3$, both rotamers) 17.86, 18.60, 27.54, 28.50, 51.16, 51.86, 54.22, 64.68, 65.04, 67.77, 68.19, 127.32, 127.70, 127.90, 128.21, 128.52, 135.56, 136.03, 139.54, 154.80 and 173.51; *m*/*z* (CI) 357 (M^+ + 18, 100%) and 340 (M^+ + 1, 12).

(3*R*)-3-[(*R*)-1-(phenyl)ethyl]aminobutyrolactone 26

The general procedure using lactone **25** (150 mg, 0.442 μmol), ammonium formate (139 mg, 2.20 mmol) and 10% Pd/C (15 mg) gave the *title compound* **26** (77 mg, 85%) as a colourless oil (Found: M^+ + H, 206.1178. $C_{12}H_{16}NO_2$ requires *M*, 206.1181); $[\alpha]_D$ +105 (*c* 1.7 in $CHCl_3$); ν_{max}/cm^{-1} 704, 766, 953, 1021, 1161, 1216, 1267, 1311, 1377, 1452, 1492, 1771, 2968 and 3323; δ_H (300 MHz, $CDCl_3$) 1.36 (3 H, d, *J* 6.6, $CHCH_3$), 1.79 (1 H, m, 4-H), 1.90 (1 H, m, 4-H), 2.13 (1 H, br s, NH), 3.34 (1 H, dd, *J* 11.0 and 8.1, 3-H), 3.95 (1 H, ddd, *J* 11.0, 9.3 and 6.1, 5-H), 4.08 (1 H, q, *J* 6.6, $CHCH_3$), 4.16–4.22 (1 H, m, 5-H) and 7.19–7.35 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 25.38, 32.54, 56.28, 58.87, 66.34, 127.78, 128.06, 129.18, 145.57 and 178.68; *m*/*z* (CI) 206 (M^+ + 1, 100%).

Butyl (2*R*,6*S*,*E*)-6-benzyloxy-2-{[benzyloxycarbonyl-[(*S*)-(1-phenylethyl)amino]}hept-4-enoate 27

The general procedure using the amino-ester **15** (575 mg, 1.40 mmol), anhydrous potassium carbonate (388 mg, 2.81 mmol) and benzyl chloroformate (257 μL, 1.82 mmol) after chromatography using hexane–ether (9 : 1) as eluent gave the *title compound* **27** (649 mg, 85%) as a colourless oil (Found: M^+ + Na, 566.2898. $C_{34}H_{41}NO_5Na$ requires *M*, 566.2883; $[\alpha]_D$ −22 (*c* 2.0 in $CHCl_3$); ν_{max}/cm^{-1} 699, 738, 975, 1073, 1210, 1308, 1430, 1453, 1496, 1703, 1738 and 2962; δ_H (300 MHz, DMSO-d_6, 80 °C) 0.96 (3 H, t, *J* 7.3, CH_3CH_2), 1.16 (3 H, d, *J* 6.3, 7-H_3), 1.35–1.43 (2 H, m, CH_3CH_2), 1.54–1.63 (2 H, m, CH_2CH_2O), 1.65 (3 H, d, *J* 7.1, $CHCH_3$), 2.09 (1 H, m, 3-H), 2.72 (1 H, m, 3-H), 3.72 (1 H, qn, *J* 6.6, 6-H), 3.92 (1 H, dd, *J* 7.4 and 5.6, 2-H), 4.00–4.13 (2 H, m, CH_2CH_2O), 4.31 and 4.42 (each 1 H, d, *J* 12.2, PhHCH), 5.03 (1 H, dd, *J* 15.6 and 7.3, 5-H), 5.16 and 5.22 (each 1 H, d, *J* 11.6, PhHCH), 5.48 (1 H, q, *J* 7.1, $CHCH_3$), 5.67 (1 H, dt, *J* 15.6 and 7.0, 4-H) and 7.32–7.50 (15 H, m, ArH); *m*/*z* (FAB) 566 (M^+ + 23, 3%) and 436 (100).

The general procedure using cbz-protected amino-ester **27** (640 mg, 1.18 mmol), ozone, methyl sulfide (259 μL, 3.53 mmol) and sodium borohydride (178 mg, 4.71 mmol) gave the alcohol ***ent*-20** that was cyclised using hydrogen chloride in methanol to afford the amidolactone ***ent*-21** (342 mg, 86%) as a white powder. A single recrystallisation from DCM–hexane gave the lactone ***ent*-21** as colourless needles, m.p. 152–153 °C; $[\alpha]_D$ −21.4 (*c* 1.6 in $CHCl_3$) (Found: C, 70.6; H, 6.25; N, 4.3%. $C_{20}H_{21}NO_4$ requires C, 70.8, H, 6.25; N, 4.5%).

The general procedure using lactone ***ent*-21** (150 mg, 0.442 μmol), ammonium formate (139 mg, 2.20 mmol) and 10% Pd/C (15 mg) gave the aminolactone ***ent*-22** (71 mg, 78%) as a colourless oil, $[\alpha]_D$ −27.9 (*c* 1.5 in $CHCl_3$).

Butyl (2*R*,6*S*,*E*)-6-benzyloxy-2-{[benzyloxycarbonyl-[(*R*)-(1-phenylethyl)amino]}hept-4-enoate 28

The general procedure using amino-ester **17** (600 mg, 1.46 mmol), anhydrous potassium carbonate (405 mg, 2.93 mmol) and benzyl chloroformate (269 μL, 1.91 mmol) after chromatography using hexane–ether (9 : 1) gave the *title compound* **28** (662 mg, 83%) as a colourless oil (Found: M^+ + Na, 566.2896. $C_{34}H_{41}NO_5Na$ requires *M*, 566.2882; $[\alpha]_D$ +34 (*c* 0.9 in $CHCl_3$); ν_{max}/cm^{-1} 699, 742, 916, 1073, 1209, 1309, 1428, 1453, 1703, 1738 and 2963; δ_H (300 MHz, DMSO-d_6, 60 °C) 0.88 (3 H, t, *J* 7.1, CH_3CH_2), 1.16–1.24 (2 H, m, CH_3CH_2), 1.26 (3 H, d, *J* 6.4, 7-H_3), 1.37 (2 H, qn, *J* 6.7, CH_2CH_2O), 1.63 (3 H, d, *J* 7.1, $CHCH_3$), 2.69 (1 H, m, 3-H), 2.90 (1 H, m, 3-H), 3.82 (1 H, t, *J* 6.3, 2-H), 3.98 (2 H, q, *J* 6.6, CH_2CH_2O), 4.03 (1 H, m, 6-H), 4.42 and 4.54 (each 1 H, d, *J* 12.3, PhHCH), 5.11 and 5.21 (1 H, d, *J* 12.5, PhHCH), 5.35 (1 H, q, *J* 7.1, $CHCH_3$), 5.51 (1 H, dd, *J* 15.4 and 6.9, 5-H), 5.77 (1 H, dt, *J* 15.4 and 7.6, 4-H) and 7.32–7.48 (15 H, m, ArH); *m*/*z* (FAB) 566 (M^+ + 23, 3%), 544 (M^+ + 1, 100) and 436 (100).

The general procedure using cbz-protected amino-ester **28** (600 mg, 1.10 mmol), ozone, methyl sulfide (243 μL, 3.31 mmol) and sodium borohydride (167 mg, 4.41 mmol) gave the alcohol **24** that was cyclised using hydrogen chloride in methanol to afford the lactone **25** as a white powder (288 mg, 77%). A single recrystallisation from DCM–hexane gave the lactone **25** as colourless needles, $[\alpha]_D$ +42.6 (*c* 1.0 in $CHCl_3$).

The general procedure using amidolactone **25** (150 mg, 0.442 μmol), ammonium formate (139 mg, 2.20 mmol) and 10% Pd/C (15 mg) gave the aminolactone **26** as a colourless oil (66 mg, 73%), $[\alpha]_D$ +103.6 (*c* 1.2 in $CHCl_3$).

Butyl (*E*)-2-(diphenylmethylimino)ethanoate 32

Butyl glyoxylate monohydrate (6.06 g, 40.9 mmol) and diphenylmethylamine (7.05 mL, 40.9 mmol) in benzene (100 mL) were heated under reflux with azeotropic removal of water for 2 h. Cooling to ambient temperature and concentration under reduced pressure gave an oil that solidified on standing. This solid was stirred with ice-cold hexane for 1 h and dried under a high vacuum (0.1 mm Hg) to afford the *title compound* **32** (10.87 g 90%) as a white powder, m.p. 46–47 °C (Found: C, 77.3; H, 7.4; N, 4.75. $C_{19}H_{21}NO_2$ requires C, 77.3; H, 7.2; N, 4.74); ν_{max}/cm^{-1} 700, 745, 860, 1028, 1062, 1199, 1293, 1366, 1392, 1453, 1494, 1601, 1648, 1721, 1749 and 2960; δ_H (300 MHz, $CDCl_3$) 0.99 (3 H, t, *J* 7.4, CH_3CH_2), 1.46 (2 H, hex, *J* 7.6, CH_3CH_2), 1.75 (2 H, qn, *J* 6.9, CH_2CH_2O), 4.33

(2 H, t, *J* 6.8, CH_2O), 5.73 (1 H, s, CH), 7.27–7.40 (10 H, m, ArH) and 7.82 (1 H, s, HC═N); δ_C (75 MHz, $CDCl_3$) 13.71, 19.08, 30.54, 65.69, 77.54, 127.54, 127.83, 128.65, 141.71, 153.71 and 163.23; *m*/*z* (CI) 296 (M^+ + 1, 80%) and 167 (100).

Butyl (*E*)-2-[(1-methyl-1-phenyl)ethylimino]ethanoate 35

Butyl glyoxylate monohydrate (2.0 g, 13.5 mmol) and 1-methyl-1-phenylethylamine (1.82g, 13.5 mmol) were dissolved in benzene (40 mL) and heated under reflux for 2 h with azeotropic removal of water. After cooling to ambient temperature and concentration under reduced pressure, the residue was dried under a high vacuum (0.5 mm Hg) for 16 h to afford the *title compound* **35** (3.30g, 99%) as a pale yellow solid (Found: M^+ + H, 248.1646. $C_{15}H_{22}NO_2$ requires *M*, 248.1657); ν_{max}/cm^{-1} 700, 766, 1027, 1065, 1102, 1197, 1253, 1293, 1345, 1386, 1463, 1494, 1648, 1721, 1749, 2873, 2934 and 2963; δ_H (300 MHz, $CDCl_3$) 0.98 (3 H, t, *J* 7.3, CH_3CH_2), 1.43 (2 H, hex, *J* 7.6, CH_3CH_2), 1.69 (6 H, s, 2 × CH_3), 1.74 (2 H, qn, *J* 7.8, CH_2CH_2O), 4.31 (2 H, m, CH_2O), 7.27–7.45 (5 H, m,ArH), 7.54 (1 H, s, HC═N); δ_C (75 MHz, $CDCl_3$) 13.71, 19.05, 29.23, 30.55, 64.52, 65.62, 126.20, 126.99, 128.42, 145.46, 150.88 and 163.809; *m*/*z* (CI) 248 (M^+ + 1, 100%) and 119 (50).

Methyl (2*R*,6*S*,*E*)-6-benzyloxy-2-[(2-nitrophenyl)sulfanylamino]-hept-4-enoate 30

Following the general procedure, tin(IV) chloride (683 mg, 2.62 mmol) in DCM (5 mL), the 4-benzyloxypent-2-enylstannane **1** (1.28 g, 2.75 mmol) in DCM (5 mL) and the imine **29** (661 mg, 2.75 mmol) in DCM (5 mL) after 12 h at −45 °C and chromatography using hexane–ether–triethylamine (60 : 39.5 : 0.5) as eluent gave the *title compound* **30** (950 mg, 87%) as a yellow oil. Preparative scale HPLC using a silica resolve cartridge, UV at 255 nm, eluent hexane–ethyl acetate (8 : 1), flow rate 2 mL min^{-1} gave the (2*R*)-epimer **30** (Found: M^+ + Na, 439.1314. $C_{21}H_{24}N_2O_5SNa$ requires *M*, 439.1304); $[\alpha]_D$ −29.5 (*c* 0.4 in $CHCl_3$); ν_{max}/cm^{-1} 699, 726, 790, 1101, 1208, 1220, 1308, 1340, 1449, 1515, 1736, 3030 and 3347; δ_H (500 MHz, methanol-d_4) 1.45 (3 H, d, *J* 6.4, 7-H_3), 2.72 (1 H, m, 3-H), 2.82 (1 H, m, 3-H), 3.78 (1 H, dd, *J* 7.3 and 5.8, 2-H), 3.92 (3 H, s, CH_3O), 4.16 (1 H, qn, *J* 6.6, 6-H), 4.58 and 4.73 (each 1 H, d, *J* 11.8, PhHC*H*), 5.74 (1 H, dd, *J* 15.4 and 7.7, 5-H), 5.93 (1 H, dt, *J* 15.4 and 7.3, 4-H), 7.43–7.50 (6 H, m, ArH), 7.83 (1 H, ddd, *J* 7.9, 7.9 and 1.5, ArH), 8.32 (1 H, dd, *J* 8.3 and 1.3) and 8.43 (1 H, dd, *J* 8.2 and 1.4, ArH); δ_H (500 MHz, $CDCl_3$) 3.30 (1 H, d, *J* 8.7, NH); δ_C (63 MHz, $CDCl_3$) 21.55, 36.35, 52.38, 63.54, 69.96, 75.49, 124.47, 124.76, 125.73, 126.06, 127.41, 127.54, 128.32, 133.74, 136.87, 138.65, 142.58, 144.82 and 173.36; *m*/*z* (FAB) 439 (M^+ + 23, 100%).

Butyl (2*R*,6*S*,*E*)- and (2*S*,6*S*,*E*)-6-benzyloxy-2-(diphenylmethyl)-aminohept-4-enoates 33 and 34

Following the general procedure, tin(IV) chloride (671 mg, 2.58 mmol) in DCM (6 mL), 4-benzyloxypent-2-enylstannane **1** (1.26 g, 2.71 mmol) in DCM (6 mL) and the imine **32** (799 mg, 2.70 mmol) in DCM (6 mL) after 12 h at −45 °C and chromatography using petrol–ether–triethylamine (93 : 6.5 : 0.5) as eluent gave the *title compounds* **33** and **34** (1.04 g, 86%) as a colourless oil, ratio **33** : **34** = 90 : 10 (^{1}H NMR) (Found: M^+ + H, 472.2848. $C_{31}H_{38}NO_3$ requires *M*, 472.2852); $[\alpha]_D$ −19 (*c* 0.7 in $CHCl_3$); ν_{max}/cm^{-1} 699, 743, 971, 1028, 1070, 1092, 1117, 1151, 1184, 1453, 1493, 1730, 2870, 2931, 2961, 3028, 3061 and 3339; δ_H (500 MHz, $CDCl_3$) major isomer 0.92 (3 H, t, *J* 7.3, CH_3CH_2), 1.26 (3 H, d, *J* 6.5, 7-H_3), 1.35 (2 H, hex, *J* 7.3, CH_3CH_2), 1.60 (2 H, qn, *J* 7.3, CH_2CH_2O), 2.17 (1 H, br s, NH), 2.33–2.49 (2 H, m, 3-H_2), 3.30 (1 H, t, *J* 6, 2-H), 3.88 (1 H, q, *J* 6.8, 6-H), 4.07–4.13 (2 H, m, CH_2CH_2O), 4.31 and 4.48 (each 1 H, d, *J* 11.8, PhHC*H*), 4.82 (1 H, s, Ph_2CH), 5.49 (1 H, dd, *J* 16.0 and 8.0, 5-H), 5.63 (1 H, dt, *J* 16.0 and 7.6, 4-H), 7.15–7.22 (2 H, m, ArH), 7.22–7.33 (9 H, m, ArH), 7.34–7.37 (2 H, m, ArH) and 7.40–7.43 (2 H, m, ArH); minor isomer 0.915 (3 H, t, *J* 7.2, CH_3CH_2), 1.25 (3 H, d, *J* 6.5, 7-H_3), 4.26 and 4.43 (each 1 H, d, *J* 11.6, PhHC*H*), 4.81 (1 H, s, Ph_2CH), 5.44 (1 H, dd, *J* 16.0 and 8.0, 5-H) and 5.59 (1 H, dt, *J* 16.0 and 7.3, 4-H); δ_C (75 MHz, $CDCl_3$) major isomer 14.40, 19.88, 22.41, 31.47, 37.27, 59.72, 65.28, 66.11, 70.53, 76.28, 127.92, 128.00, 128.06, 128.31, 128.38, 128.53, 129.03, 129.21, 129.25, 136.27, 139.56, 143.50, 144.93 and 175.48; *m*/*z* (CI) 472 (M^+ + 1, 100%).

Butyl (2*R*,6*S*,*E*)- and (2*S*,6*S*,*E*)-6-benzyloxy-2-(1-methyl-1-phenylethyl)aminohept-4-enoates 36 and 37

Following the general procedure, tin(IV) chloride (672 mg, 2.58 mmol) in DCM (7 mL), 4-benzyloxypent-2-enylstannane **1** (1.26 g, 2.71 mmol) in DCM (7 mL) and imine **35** (670 mg, 2.71 mmol) in DCM (7 mL) after 12 h at −45 °C and chromatography using petrol–ether–triethylamine (85 : 14.5 : 0.5) as eluent gave the *title compounds* **36** and **37** (852 mg, 78%) as a colourless oil, ratio **36** : **37** = 91 : 9 (^{1}H NMR) (Found: M^+ + H, 424.2872. $C_{27}H_{38}NO_3$ requires *M*, 424.2852); ν_{max}/cm^{-1} 699, 735, 765, 971, 1072, 1174, 1445, 1453, 1731, 2969 and 3334; δ_H (300 MHz, $CDCl_3$) major isomer 0.94 (3 H, t, *J* 7.3, CH_3CH_2), 1.30 (3 H, d, *J* 6.6, 7-H_3), 1.35 (2 H, hex, *J* 7.7, CH_3CH_2), 1.45 and 1.47 (each 3 H, s, CH_3), 1.57 (2 H, qn, *J* 7.5, CH_2CH_2O), 2.29–2.34 (2 H, m, 3-H_2), 3.12 (1 H, t, *J* 6.5, 2-H), 3.90 (1 H, qn, *J* 6.8, 6-H), 4.00 (2 H, t, *J* 6.7, CH_2CH_2O), 4.37 and 4.55 (each 1 H, d, *J* 11.9, PhHC*H*), 5.49 (1 H, dd, *J* 15.3 and 7.1, 5-H), 5.61 (1 H, dt, *J* 15.3 and 6.3, 4-H), 7.24–7.40 (8 H, m, ArH) and 7.51–7.53 (2 H, m, ArH); minor isomer 1.28 (3 H, d, *J* 6.7, 7-H_3), 3.11 (1 H, t, *J* 6.5, 2-H), 3.95–4.05 (2 H, m, CH_2CH_2O), 4.39 and 4.58 (each 1 H, d, *J* 11.9, PhHC*H*) and 5.45 (1 H, dd, *J* 15.3 and 7.0, 5-H); δ_C (75 MHz, $CDCl_3$) major isomer 13.74, 19.17, 21.71, 28.15, 30.61, 31.33, 38.48, 56.28, 64.61, 69.78, 75.64, 126.25, 126.51, 127.40, 127.70, 128.06, 128.30, 128.36, 135.18, 138.93, 147.48 and 176.36; minor isomer 38.52, 56.34, 135.06 and 176.44; *m*/*z* (CI) 424 (M^+ + 1, 100%).

Methyl (2*R*,6*S*,*E*)-6-benzyloxy-2-(methoxycarbonylamino)hept-4-enoate 38

Following the general procedures, following deprotection of the sulfanylamines **30** (and **31**) (180 mg, 0.432 μmol, 9 : 1) using

hydrogen chloride in methanol, treatment of the free amines with anhydrous potassium carbonate (138 mg, 0.864 μmol) and methyl chloroformate (67 μl, 0.867 μmol), after chromatography using hexane–ether (65 : 35) as eluent gave the *title compound* **38** (121 mg, 87%); the minor (2*S*)-epimer was not detected (Found: $M^+ + NH_4$, 339.1913. $C_{17}H_{27}N_2O_5$ requires *M*, 339.1920); $[\alpha]_D$ −79 (*c* 0.43 in $CHCl_3$); ν_{max}/cm^{-1} 699, 738, 1065, 1211, 1355, 1441, 1453, 1522, 1726, 2954 and 3338; δ_H (300 MHz, $CDCl_3$, 50 °C) 1.23 (3 H, d, *J* 6.4, 7-H_3), 2.40–2.64 (2 H, m, 3-H_2), 3.66 and 3.72 (each 3 H, s, CH_3O), 3.88 (1 H, m, 2-H), 4.35 (1 H, d, *J* 12.0, PhHC*H*), 4.41 (1 H, m, 6-H), 4.51 (1 H, d, *J* 12, PhHC*H*), 5.16 (1 H, br s, NH), 5.46–5.53 (2 H, m, 4-H and 5-H) and 7.22–7.33 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 21.61, 35.41, 52.37, 52.45, 53.50, 69.89, 75.20, 125.82, 127.48, 127.69, 128.38, 137.00, 138.69, 156.30 and 172.19; *m*/*z* (CI) 339 (M^+ + 1, 100%) and 214 (70).

(*R*)-3-(Methoxycarbonylamino)butyrolactone 39

Following the general procedures, the hept-2-enoate **38** (125 mg, 0.389 μmol), ozone, methyl sulfide (86 μL, 1.17 mmol) and sodium borohydride (59 mg, 1.56 mmol) gave the corresponding alcohol that was cyclised using glacial acetic acid in chloroform with chromatography using ethyl acetate–hexane–triethylamine (60 : 39.5 : 0.5) as eluent to give the *title compound* **39** (45 mg, 73%) as a white powder, m.p. 95–96 °C (lit.[14] 95–97 °C) (Found: C, 45.6; H, 5.9; N, 8.7. $C_6H_9NO_4$ requires C, 45.3; H, 5.7; N, 8.8); $[\alpha]_D$ +29.7 (*c* 0.7 in MeOH) [lit.[14] for the (*S*)-enantiomer −39.5 (*c* 1 in MeOH)]; ν_{max}/cm^{-1} 1019, 1063, 1177, 1197, 1257, 1293, 1381, 1532, 1713, 1777, 2958 and 3336; δ_H (300 MHz, $CDCl_3$) 2.27 and 2.78 (each 1 H, m, 4-H), 3.74 (3 H, s, CH_3O), 4.29 (1 H, m, 3-H), 4.40–4.51 (2 H, m, 5-H_2) and 5.50 (1 H, br s, NH); δ_C (75 MHz, $CDCl_3$) 30.22, 50.49, 52.66, 65.80, 156.80 and 175.19; *m*/*z* (CI) 181 (M^+ + 18, 90%) and 164 (M^+ + 1, 100).

Methyl (2*R*,6*S*,*E*)-2-acetamido-6-benzyloxyhept-4-enoate 40

Following the general procedures, following deprotection of the sulfanylamines **30** (and **31**) (800 mg, 1.92 mmol, 9 : 1) using hydrogen chloride in methanol and treatment of the free amines with acetic anhydride (272 μL, 2.88 mmol), triethylamine (803 μl, 5.76 mmol) and DMAP (5 mg, 41 μmol), after chromatography using hexane–ethyl acetate (1 : 1) as eluent, gave the *title compound* **40** (480 mg, 82%) as a colourless oil; the (2*S*)-epimer was not detected (Found: M^+ + H, 306.1713. $C_{17}H_{24}NO_4$ requires *M*, 306.1705); $[\alpha]_D$ −78.5 (*c* 0.93 in $CHCl_3$); ν_{max}/cm^{-1} 699, 738, 973, 1072, 1089, 1213, 1372, 1438, 1544, 1657, 1746, 2974 and 3287; δ_H (300 MHz, $CDCl_3$) 1.28 (3 H, d, *J* 6.3, 7-H_3), 2.03 (3 H, s, CH_3CO), 2.52 (1 H, m, 3-H), 2.66 (1 H, m, 3-H), 3.78 (3 H, s, CH_3O), 3.92 (1 H, m, 6-H), 4.40 and 4.56 (each 1 H, d, *J* 11.9, PhHC*H*), 4.73 (1 H, m, 2-H), 5.53–5.55 (2 H, m, 4-H and 5-H), 6.11 (1 H , d, *J* 7.4, NH) and 7.28–7.40 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 21.61, 23.17, 35.20, 51.92, 52.46, 69.84, 75.22, 125.93, 127.49, 127.61, 128.41, 136.84, 138.68, 169.61 and 172.30; *m*/*z* (CI) 323 (M^+ + 18, 6.5%), 306 (M^+ + 1, 4.5) and 198 (100).

Methyl (2*R*,6*S*)-2-acetamido-6-hydroxyheptanoate 41

Following the general procedure for transfer hydrogenation, acetamide **40** (90 mg, 0.295 μmol) gave a yellow oil that was dissolved in chloroform, absorbed on to silica and the resulting powder applied to a column of silica gel. Elution with chloroform–methanol (99 : 1) gave methyl (*R*)-2-acetamidoheptanoate **42** (3 mg, 5%), as a colourless oil (Found: M^+ + H, 202.1442. $C_{10}H_{20}NO_3$ requires *M*, 202.1443); $[\alpha]_D$ −29.6 (*c* 0.6 in $CHCl_3$); ν_{max}/cm^{-1} 1153, 1180, 1211, 1374, 1437, 1546, 1656, 1747, 2861, 2955 and 3289; δ_H (300 MHz, $CDCl_3$) 0.90 (3 H, t, *J* 6.7, 7-H_3), 1.21–1.40 (6 H, m, 4-H_2, 5-H_2 and 6-H_2), 1.68 and 1.80 (each 1 H, m, 3-H), 2.05 (3 H, s, CH_3CO), 3.77 (3 H, s, CH_3O), 4.63 (1 H, m, 2-H) and 6.10 (1 H, d, *J* 7.0, NH); δ_C (75 MHz, $CDCl_3$) 13.94, 22.41, 23.18, 24.85, 31.35, 32.48, 52.17, 52.31, 169.77 and 173.33; *m*/*z* (CI) 219 (M^+ + 18, 20%) and 202 (M^+ + 1, 100). Further elution with chloroform–methanol (96 : 4) gave the *title compound* **41** (51 mg, 79%) as a colourless oil containing *ca.* of its epimer at C(2) (Found: M^+ + H, 218.1392. $C_{10}H_{20}NO_4$ requires *M*, 218.1392); ν_{max}/cm^{-1} 1038, 1147, 1213, 1375, 1438, 1549, 1659, 1745, 2958, 3073 and 3290; δ_H (300 MHz, $CDCl_3$) 1.20 (3 H, d, *J* 6.2, 7-H_3), 1.30–1.91 (6 H, m, 3-H_2, 4-H_2 and 5-H_2), 2.01 (1 H, br s, OH), 2.03 (3 H, s, CH_3CO), 3.77 (3 H, s, CH_3O), 3.76 (1 H, m, 6-H), 4.63 (1 H, m, 2-H) and 6.30 (1 H, d, *J* 7.9, NH); δ_C (75 MHz, $CDCl_3$) 21.48, 23.16, 23.69, 32.40, 38.44, 52.04, 52.41, 67.52, 170.07 and 173.21; minor (2*S*)-epimer 23.56, 32.48 and 67.60; *m*/*z* (CI) 218 (M^+ + 1, 100%).

Methyl (2*R*,6*S*)-2-acetamido-6-acetoxyheptanoate 43

Following the general procedure for acetylation, the alcohol **41** (22 mg, 0.101 μmol, 9 : 1), triethylamine (42 μL, 0.301 μmol), acetic anhydride (16 mg, 0.157 μmol) and DMAP (0.5 mg, 4 μmol) after chromatography using chloroform–methanol (99 : 1) as eluent gave the *title compound* **43** (25 mg, 95%) as a colourless oil containing *ca.* 10% of its (2*S*)-epimer (Found: M^+ + H, 260.1503. $C_{12}H_{22}NO_5$ requires *M*, 260.1498); ν_{max}/cm^{-1} 803, 1023, 1092, 1150, 1251, 1373, 1439, 1540, 1657, 1734, 2866, 2953 and 3283; δ_H (500 MHz, $CDCl_3$) 1.22 (3 H, d, *J* 6.3, 7-H_3), 1.20–1.84 (6 H, m, 3-H_2, 4-H_2 and 5-H_2), 1.99 (6 H, s, 2 × CH_3CO), 3.71 (3 H, s, CH_3O), 4.55 (1 H, dt, *J* 5.4 and 7.7, 2-H), 4.85 (1 H, m, 6-H) and 6.03 (1 H, d, *J* 7.7, NH); δ_C (75 MHz, $CDCl_3$) 20.03, 21.15, 21.36, 23.15, 32.08, 35.34, 52.02, 52.39, 70.28, 169.87, 170.86 and 173.04; minor (2*S*)-epimer 19.93, 32.29 and 70.57; *m*/*z* (CI) 277 (M^+ + 18, 70%) and 260 (M^+ + 1, 100).

Methyl (2*R*,6*S*,*E*)-2-(diphenylmethyl)amino-6-benzyloxyhept-4-enoate 44

Anhydrous potassium carbonate (293 mg, 2.12 mmol) was added to a mixture of the butyl esters **33** and **34** (200 mg, 0.424 μmol, 9 : 1) in methanol (5.6 mL) and water (1.4 mL) and the mixture was heated under reflux for 16 h. After cooling to ambient temperature and concentration under reduced pressure, the residue was dissolved in saturated aqueous sodium hydrogen carbonate. This solution was washed twice with ether, the aqueous layer was acidified using hydrogen chloride (1 M) and

the solution extracted with ether. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure to ~10 mL. An excess of diazomethane in ether was added and the yellow solution stirred at ambient temperature for 30 min before glacial acetic acid was added dropwise until a colourless solution was obtained. Water (20 mL) was added and the organic phase was washed with saturated aqueous sodium hydrogen carbonate and dried ($MgSO_4$). Silica was added (*ca*. 1 g) and the mixture was concentrated under reduced pressure. The ensuing powder was applied to a column of silica gel. Chromatography using hexane–ether (9 : 1) as eluent gave the *title compound* **44** (166 mg, 91%) as a colourless oil (Found: M^+ + H, 430.2374. $C_{28}H_{32}NO_3$ requires *M*, 430.2382); ν_{max}/cm^{-1} 701, 743, 974, 1029, 1072, 1200, 1452, 1493, 1735, 2859, 3028 and 3330; δ_H (300 MHz, $CDCl_3$) 1.33 (3 H, d, *J* 6.3, 7-H_3), 2.23 (1 H, br s, NH), 2.45–2.53 (2 H, m, 3-H_2), 3.39 (1 H, t, *J* 6.3, 2-H), 3.75 (3 H, s, CH_3O), 3.95 (1 H, m, 6-H), 4.37 and 4.55 (each 1 H, d, *J* 11.9, PhHC*H*), 4.88 (1 H, s, Ph_2CH), 5.54 (1 H, dd, *J* 15.4 and 7.5, 5-H), 5.68 (1 H, dt, *J* 15.4 and 7.9, 4-H) and 7.22–7.49 (15 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 21.76, 36.59, 51.75, 59.01, 65.40, 69.81, 75.54, 127.26, 127.30, 127.40, 127.57, 127.64, 127.70, 128.36, 128.54, 128.58, 135.65, 138.82, 142.74, 144.14 and 175.24; *m*/*z* (CI) 430 (M^+ + 1, 100%).

Following the general procedure for transfer hydrogenation, the 2-(diphenylmethylamino)heptenoate **44** (65 mg, 0.151 μmol) gave an oil that was acylated using triethylamine (127 μL, 0.911 μmol), acetic anhydride (46 mg, 0.451 μmol) and DMAP (0.5 mg, 4 μmol) to give, after chromatography using chloroform–methanol (99 : 1) as eluent, methyl (*R*)-2-acetamidoheptanoate **42** (2 mg, 7%) as a colourless oil. Further elution using chloroform–methanol (96 : 4) gave the 2-acetamido-6-acetoxyheptanoate **43** (31 mg, 80%) as a colourless oil containing *ca.* 10% of its (2*S*)-epimer.

Butyl (2*S*,6*R*,*E*)- and (2*R*,6*R*,*E*)-7-benzyloxy-6-methyl-2-[(*R*)-(1-phenylethyl)]aminohept-4-enoates 84 and 85

The general procedure using tin(IV) chloride (833 mg, 3.20 mmol) in DCM (9 mL), 5-benzyloxypentenylstannane **80** (1.61 g, 3.36 mmol) in DCM (9 mL) and the imine (***R*)-11** (783 mg, 3.36 mmol) in DCM (9 mL) after 12 h at −45 °C and chromatography using petrol–ether–triethylamine (90 : 9.5 : 0.5) as eluent gave the *title compounds* **84** and **85** (1.03 g, 76%) as a colourless oil, **84** : **85** = 95 : 5 (^{1}H NMR). Further chromatography using petrol–ether (9 : 1) as the eluent gave a sample of the major (2*S*)-epimer **84** as a colourless oil (Found: M^+ + H, 424.2858. $C_{27}H_{38}NO_3$ requires *M*, 424.2851); $[\alpha]_D$ +28 (*c* 1.5 in $CHCl_3$); ν_{max}/cm^{-1} 699, 738, 970, 1028, 1098, 1179, 1453, 1733, 2961 and 3335; δ_H (500 MHz, $CDCl_3$) 0.89 (3 H, t, *J* 7.3, CH_3CH_2), 1.00 (3 H, d, *J* 6.6, 6-CH_3), 1.27–1.34 (2 H, m, CH_3CH_2), 1.31 (3 H, d, *J* 6.4, PhCHCH_3), 1.52 (2 H, qn, *J* 7.3, CH_2CH_2O), 1.76 (1 H, br s, NH), 2.30–2.38 (2 H, m, 3-H_2), 2.44 (1 H, m, 6-H), 3.23 (1 H, dd, *J* 8.8 and 7.1, 7-H), 3.30 (1 H, t, *J* 6.4, 2-H), 3.32 (1 H, dd, *J* 9.4 and 6.4, 7-H), 3.76 (1 H, q, *J* 6.4, PhC*H*CH_3), 3.91–3.98 (2 H, m, CH_2CH_2O), 4.46 and 4.48 (each 1 H, d, *J* 12.2, PhHC*H*), 5.42 (1 H, dt, *J* 15.6 and 6.4, 4-H), 5.46 (1 H, dd, *J* 15.6 and 6.4, 5-H) and 7.24–7.34 (10 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 13.70, 17.21, 19.15, 23.21, 30.67, 36.40, 36.93, 56.14, 59.04, 64.36, 72.95, 75.31, 124.71, 126.82, 127.09, 127.48, 127.56, 128.34, 128.40, 136.58, 138.64, 145.28 and 174.63; *m*/*z* (CI) 424 (M^+ + 1, 100%); minor epimer **85** δ_H (500 MHz, $CDCl_3$) 2.24–2.27 (m, 3-H_2), 3.01 (t, *J* 6.4, 2-H) and 3.68 (q, *J* 6.4, PhC*H*CH_3).

Butyl (2*S*,6*R*,*E*)- and (2*R*,6*R*,*E*)-7-benzyloxy-6-methyl-2-[(*S*)-(1-phenylethyl)]aminohept-4-enoate 86 and 88

The general procedure using tin(IV) chloride (679 mg, 2.61 mmol) in DCM (8 mL), 5-benzyloxypentenylstannane **80** (1.31 g, 2.73 mmol) in DCM (8 mL) and the imine (***S*)-11** (638 mg, 2.73 mmol) in DCM (8 mL) after 12 h at −45 °C and chromatography using petrol–ether–triethylamine (90 : 9.5 : 0.5) as eluent gave the *title compounds* **86** and **88** (762 mg, 69%) as a colourless oil, **86** : **88** = 60 : 40 (^{1}H NMR). Further chromatography using petrol–ether (9 : 1) as the eluent gave a sample of the major (2*S*)-epimer **86** as a colourless oil (Found: M^+ + H, 424.2856. $C_{27}H_{38}NO_3$ requires *M*, 424.2851); $[\alpha]_D$ −40 (*c* 2 in $CHCl_3$); ν_{max}/cm^{-1} 700, 737, 971, 1028, 1098, 1182, 1453, 1604, 1732, 2960 and 3329; δ_H (500 MHz, $CDCl_3$) 0.91 (3 H, t, *J* 7.5, CH_3CH_2), 1.01 (3 H, d, *J* 6.6, 6-CH_3), 1.29 (3 H, d, *J* 6.6, PhCHCH_3), 1.34 (2 H, hex, *J* 7.5, CH_3CH_2), 1.57 (2 H, qn, *J* 6.8, CH_2CH_2O), 1.72 (1 H, br s, NH), 2.24–2.27 (2 H, m, 3-H_2), 2.43 (1 H, sep, *J* 6.6, 6-H), 3.02 (1 H, t, *J* 6.4, 2-H), 3.22 (1 H, dd, *J* 8.8 and 7.5, 7-H), 3.32 (1 H, dd, *J* 9.2 and 6.4, 7-H), 3.68 (1 H, q, *J* 6.6, PhC*H*CH_3), 4.03–4.12 (2 H, m, CH_2CH_2O), 4.47 and 4.49 (each 1 H, d, *J* 13.3, PhHC*H*), 5.36 (1 H, dt, *J* 15.6 and 6.8, 4-H), 5.42 (1 H, dd, *J* 15.6 and 6.4, 5-H) and 7.24–7.33 (10 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 13.78, 17.16, 19.21, 23.26, 30.78, 36.82, 37.13, 56.56, 58.92, 64.28, 72.88, 75.21, 124.78, 126.67, 126.75, 127.32, 127.40, 128.18, 136.01, 138.42, 144.88 and 175.10; *m*/*z* (CI) 424 (M^+ + 1, 100%); minor epimer **88** δ_H (500 MHz, $CDCl_3$) 0.89 (t, *J* 7.5, CH_3CH_2), 1.00 (d, *J* 6.6, 6-CH_3), 1.31 (d, *J* 6.6, PhCHCH_3), 1.52 (qn, *J* 7.6, CH_2CH_2O), 2.33–2.36 (m, 3-H_2), 3.24 (t, *J* 6.4, 2-H), 3.31 (dd, *J* 9.1 and 7.1, 7-H), 3.75 (q, *J* 6.6, PhC*H*CH_3) and 3.95 (t, *J* 6.6, CH_2CH_2O); δ_C (75 MHz, $CDCl_3$) 17.35, 30.68, 36.44, 36.99, 56.12, 59.03, 124.56, 126.84, 126.93, 136.48, 145.01 and 174.39.

Butyl (2*S*,6*R*,*E*)- and (2*R*,6*R*,*E*)-7-benzyloxy-6-methyl-2-{(benzyloxycarbonyl)-[(*S*)-(1-phenyl)ethyl]amino}hept-4-enoate 87 and 89

The general procedure for protection of amines using the amino-esters **86** and **88** (326 mg, 0.770 μmol, **86** : **88** = 60 : 40), anhydrous potassium carbonate (213 mg, 1.54 mmol) and benzyl chloroformate (141 μL, 0.926 μmol) after chromatography using petrol–ether (98 : 2 to 9 : 1) as eluent gave the *title compounds* **87** and **89** (361 mg, 84%) as a colourless oil. Samples of each isomer as colourless oils were obtained by preparative HPLC (Rainin Dynamax silica column, UV at 254 nm, eluent hexane–ethyl acetate 15 : 1, flow rate 15 mL min^{-1}): (2*R*)-epimer **89** (less polar, 38% of the mixture) (Found: M^+ + Na, 580.3059. $C_{35}H_{43}NO_5Na$ requires *M*, 580.3039); $[\alpha]_D$ −19 (*c* 1.4 in $CHCl_3$); ν_{max}/cm^{-1} 698, 737, 1081, 1212, 1290, 1427, 1453, 1703, 1739 and 2961; δ_H (300 MHz, DMSO-d_6, 95 °C) 0.83

(3 H, d, *J* 6.9, 6-CH_3), 0.87 (3 H, t, *J* 7.4, CH_3CH_2), 1.30 (2 H, hex, *J* 7.5, CH_3CH_2), 1.49 (2 H, qn, *J* 7.3, CH_2CH_2O), 1.53 (3 H, d, *J* 7, PhCHCH_3), 1.98 and 2.17 (each 1 H, m, 3-H), 2.57 (1 H, m, 6-H), 3.12 (1 H, dd, *J* 9.2 and 7.0, 7-H), 3.20 (1 H, dd, *J* 9.2 and 6.1, 7-H), 3.76 (1 H, dd, *J* 7.1 and 5.9, 2-H), 3.91–4.04 (2 H, m, CH_2CH_2O), 4.43 (2 H, s, $PhCH_2$), 4.96–4.98 (2 H, m, 4-H and 5-H), 5.06 and 5.11 (each 1 H, d, *J* 11.8, PhHC*H*), 5.35 (1 H, q, *J* 7, PhC*H*CH_3) and 7.23–7.37 (15 H, m, ArH); δ_H (300 MHz, toluene-d_8, 90 °C) 5.01 (1 H, dd, *J* 15.2 and 6.8, 5-H), 5.14 (1 H, dt, *J* 15.2 and 7.0, 4-H); *m*/*z* (CI) 575 (M^+ + 18, 100%), 558 (M^+ + 1, 50) and 454 (100); (2*S*)-epimer **87** (more polar, 62% of the mixture) (Found: M^+ + H, 558.3242. $C_{35}H_{44}NO_5$ requires *M*, 558.3219); $[\alpha]_D$ −34 (*c* 1.3 in $CHCl_3$); ν_{max}/cm^{-1} 699, 738, 1027, 1077, 1210, 1296, 1428, 1453, 1496, 1702, 1739 and 2959; δ_H (300 MHz, DMSO-d_6, 95 °C) 0.81 (3 H, t, *J* 7.2, CH_3CH_2), 0.96 (3 H, d, *J* 7.0, 6-CH_3), 1.16 (2 H, hex, *J* 7.3, CH_3CH_2), 1.31 (2 H, qn, *J* 7.0, CH_2CH_2O), 1.52 (3 H, d, *J* 7.1, PhCHCH_3), 2.40 and 2.55 (each 1 H, m, 3-H), 2.74 (1 H, m, 6-H), 3.26 (1 H, dd, *J* 9.1 and 7.0, 7-H), 3.34 (1 H, dd, *J* 9.1 and 6.3, 7-H), 3.75 (2 H, t, *J* 6.8, CH_2CH_2O), 3.91 (1 H, dd, *J* 6.6 and 6.6, 2-H), 4.46 (2 H, s, $PhCH_2$), 5.03 and 5.11 (each 1 H, d, *J* 12.0, PhHC*H*), 5.23 (1 H, q, *J* 7.1, PhC*H*CH_3), 5.35–5.51 (2 H, m, 4-H and 5-H) and 7.21–7.38 (15 H, m, ArH); *m*/*z* (CI) 575 (M^+ + 18, 30%), 558 (M^+ + 1, 35), 454 (70) and 91 (100).

Methyl (2*S*,6*R*,*E*)-7-benzyloxy-6-methyl-2-(2-nitrophenylsulfanyl)aminohept-4-enoate 90

The general procedure using tin(IV) chloride (697 mg, 2.68 mmol) in DCM (5 mL), 5-benzyloxypentenylstannane **80** (1.35 g, 2.82 mmol) in DCM (5 mL) and imine **29** (675 mg, 1.83 mmol) in DCM (5 mL) after 12 at −45 °C and chromatography using hexane–ether–triethylamine (60 : 39.5 : 0.5) as eluent gave the *title compound* **90** (850 mg, 74%) as a yellow oil, only the one diastereoisomer was detected by ^1H NMR (Found: M^+ + H, 431.1650. $C_{22}H_{27}N_2O_5S$ requires *M*, 431.1641); $[\alpha]_D$ +14 (*c* 1.05 in $CHCl_3$); ν_{max}/cm^{-1} 699, 736, 788, 851, 973, 1098, 1207, 1305, 1337, 1449, 1511, 1565, 1592, 1740, 2857, 2955 and 3330; δ_H (300 MHz, $CDCl_3$) 1.09 (3 H, d, *J* 6.9, 6-CH_3), 2.49–2.70 (3 H, m, 3-H_2 and 6-H), 3.29–3.41 (3 H, m, 2-H, 7-H and NH), 3.61 (1 H, m, 7-H), 3.80 (3 H, s, CH_3O), 4.55 (2 H, s, $PhCH_2$), 5.50 (1 H, dt, *J* 15.0 and 7.0, 4-H), 5.64 (1 H, dd, *J* 15.0 and 6.8, 5-H), 7.28 (1 H, ddd, *J* 7.5, 7.5 and 1.0, ArH), 7.29–7.39 (5 H, m, ArH), 7.62 (1 H, ddd, *J* 7.5, 7.5 and 1.0, ArH), 8.12 (1 H, dd, *J* 7.5 and 1.0, ArH) and 8.30 (1 H, dd, *J* 7.5 and 1.0, ArH); δ_C (75 MHz, $CDCl_3$) 17.04, 36.84, 37.04, 52.26, 63.70, 73.03, 75.10, 123.60, 123.64, 124.69, 125.73, 127.54, 127.60, 128.35, 133.75, 138.27, 138.48, 142.59, 145.14 and 173.70; *m*/*z* (CI) 448 (M^+ + 18, 10%), 431 (M^+ + 1, 80) and 278 (100).

Butyl (2*S*,6*R*,*E*)-2-(diphenylmethyl)amino-7-benzyloxy-6-methylhept-4-enoate 92

The general procedure using tin(IV) chloride (455 mg, 1.75 mmol) in DCM (5 mL), 5-benzyloxypentenylstannane **80** (879 mg, 1.83 mmol) in DCM (5 mL) and imine **32** (542 mg, 1.83 mmol) in DCM (5 mL) after 12 h at −45 °C and chromatography using petrol–ether–triethylamine (93 : 6.5 : 0.5) as eluent gave the *title compound* **92** (660 mg, 78%) as a colourless oil, only the one diastereoisomer being detected by ^1H NMR (Found: M^+ + H, 486.3004. $C_{32}H_{40}NO_3$ requires *M*, 486.3008); $[\alpha]_D$ +1.9 (*c* 0.6 in $CHCl_3$); ν_{max}/cm^{-1} 700, 744, 971, 1028, 1099, 1183, 1454, 1494, 1600, 1731, 2959 and 3328; δ_H (300 MHz, $CDCl_3$) 0.98 (3 H, t, *J* 7.3, CH_3CH_2), 1.07 (3 H, d, *J* 6.8, 6-CH_3), 1.40 (2 H, hex, *J* 7.8, CH_3CH_2), 1.65 (2 H, qn, *J* 8.1, CH_2CH_2O), 2.21 (1 H, br s, NH), 2.40–2.47 (2 H, m, 3-H_2), 2.51 (1 H, m, 6-H), 3.26–3.32 (2 H, m, 2-H and 7-H), 3.39 (1 H, dd, *J* 9.1 and 6.3, 7-H), 4.15 (2 H, t, *J* 6.6, CH_2CH_2O), 4.53 (2 H, s, $PhCH_2$), 4.86 (1 H, s, Ph_2CH), 5.51–5.54 (2 H, m, 4-H and 5-H) and 7.21–7.48 (15 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 13.76, 17.20, 19.22, 30.82, 36.93, 36.98, 59.28, 64.45, 65.42, 72.99, 75.35, 124.96, 125.04, 127.20, 127.40, 127.51, 127.60, 127.69, 128.38, 128.50, 128.54, 136.42, 138.70, 142.96, 144.36 and 175.01; *m*/*z* (CI) 486 (M^+ + 1, 100%).

Butyl (2*S*,6*R*,*E*)-7-benzyloxy-6-methyl-2-{(benzyloxycarbonyl)-[(*R*)-1-phenylethyl]amino}hept-4-enoate 94

The general procedure using the 2-amino-ester **84** (800 mg, 1.89 mmol), anhydrous potassium carbonate (522 mg, 3.78 mmol) and benzyl chloroformate (346 μL, 2.45 mmol) after chromatography using petrol–ether (9 : 1 to 4 : 1) as eluent gave the *title compound* **94** (916 mg, 87%) as a colourless oil (Found: M^+ + Na, 580.3053. $C_{35}H_{43}NO_5Na$ requires *M*, 580.3039); $[\alpha]_D$ +17 (*c* 1.6 in $CHCl_3$); ν_{max}/cm^{-1} 690, 773, 1077, 1210, 1250, 1292, 1427, 1453, 1702, 1739 and 2969; δ_H (300 MHz, DMSO-d_6, 95 °C) 0.94 (3 H, d, *J* 6.7, 6-CH_3), 0.97 (3 H, t, *J* 7.3, CH_3CH_2), 1.40 (2 H, hex, *J* 7.5, CH_3CH_2), 1.60 (2 H, qn, *J* 7.8, CH_2CH_2O), 1.64 (3 H, d, *J* 7.1, PhCHCH_3), 2.10 and 2.27 (each 1 H, m, 3-H), 2.67 (1 H, m, 6-H), 3.22 (1 H, dd, *J* 9.3 and 7.0, 7-H), 3.30 (1 H, dd, *J* 9.3 and 6.1, 7-H), 3.88 (1 H, dd, *J* 7.3 and 6.1, 2-H), 4.01–4.14 (2 H, m, CH_2CH_2O), 4.53 (2 H, s, $PhCH_2$), 5.03–5.05 (2 H, m, 4-H and 5-H), 5.19 (2 H, s, $PhCH_2$), 5.45 (1 H, q, *J* 7.1, PhC*H*CH_3) and 7.33–7.49 (15 H, m, ArH); *m*/*z* (CI) 575 (M^+ + 18, 100%), 558 (M^+ + 1, 70) and 454 (100).

The general procedure using cbz-ester **94** (800 mg, 1.43 mmol), ozone, methyl sulfide (0.316 mL, 4.30 mmol) and sodium borohydride (217 mg, 5.74 mmol) gave an alcohol that was cyclised using hydrogen chloride in methanol to afford the lactone **21** (389 mg, 80%) as a white powder. A single recrystallisation from DCM–hexane gave the lactone **21** as colourless needles: m.p. 152–153 °C; $[\alpha]_D$ +22 (*c* 0.8 in $CHCl_3$).

The general procedure for transfer hydrogenolysis using this lactone **21** (120 mg, 0.354 μmol), ammonium formate (111 mg, 1.76 mmol) and 10% Pd/C (12 mg) gave the amino-lactone **22** (59 mg, 82%) as a colourless oil, $[\alpha]_D$ +32 (*c* 1.8 in $CHCl_3$).

Methyl (2*S*,6*R*,*E*)-7-benzyloxy-2-(methoxycarbonyl)amino-6-methylhept-4-enoate 95

The general procedure for removal of *o*-nitrophenylsulfanylthio groups and *N*-methoxycarbonylation using the ester **90** (600 mg, 1.39 mmol), anhydrous potassium carbonate (385 mg, 2.79 mmol) and methyl chloroformate (215 μL, 2.78 mmol)

after chromatography using hexane–ethyl acetate (4 : 1) as eluent gave the *title compound* **95** (360 mg, 77%) as a colourless oil (Found (M^+ + H, 336.1812. $C_{18}H_{26}NO5$ requires *M*, 336.1811); $[\alpha]_D$ +19 (*c* 2.8 in $CHCl_3$); ν_{max}/cm^{-1} 699, 739, 973, 1065, 1210, 1356, 1451, 1519, 1727, 2855, 2955 and 3341; δ_H (300 MHz, $CDCl_3$) major rotamer 0.96 (3 H, d, *J* 6.8, 6-CH_3), 2.40–2.50 (3 H, m, 3-H_2 and 6-H), 3.21–3.31 (2 H, m, 7-H_2), 3.61 and 3.70 (3 H, s, CH_3O), 4.36 (1 H, m, 2-H), 4.48 (2 H, s, $PhCH_2$), 5.25 (1 H, d, *J* 8.1, NH), 5.30 (1 H, dt, *J* 15.6 and 7.1, 4-H), 5.46 (1 H, dd, *J* 15.6 and 7.3, 5-H) and 7.22–7.32 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) major rotamer 17.02, 35.65, 37.03, 52.26, 53.42, 65.85, 72.97, 75.04, 123.11, 127.51, 127.58, 128.35, 138.41, 138.55, 156.40 and 172.37; *m*/*z* (CI) 353 (M^+ + 18, 10%) and 336 (M^+ + 1, 100).

The general procedure using the carbamate **95** (200 mg, 0.596 μmol), ozone, methyl sulfide (131 μL, 1.78 mmol) and sodium borohydride (90 mg, 2.38 mmol) gave an alcohol that was cyclised using glacial acetic acid in chloroform to afford, after chromatography using ethyl acetate–hexane–triethylamine (60 : 39.5 : 0.5) as eluent, the 3-(methoxycarbonyl)aminolactone (***S*)-39** (59 mg, 62%) as a white powder, $[\alpha]_D$ −39 (*c* 2 in MeOH).[14]

(2*S*,6*R*,*E*)-2-(Diphenylmethyl)amino-7-benzyloxy-6-methylhept-4-en-1-ol 96

Diisobutylaluminium hydride in hexanes (1 M, 3 mL, 3 mmol) was added to the ester **92** (490 mg, 1.01 mmol) in DCM (15 mL) at −78 °C and the mixture was stirred to ambient temperature over a period of 1 h. After cooling to −78 °C, saturated aqueous ammonium chloride (750 μL) was added and the mixture was stirred vigorously to ambient temperature, then filtered (Celite) and absorbed onto silica. The resulting white powder was applied to a column of silica gel and elution with hexane–ether (3 : 2) gave the *title compound* **96** (386 mg, 92%) as a colourless oil (Found: M^+ + H, 416.2600. $C_{28}H_{34}NO_2$ requires *M*, 416.2590); $[\alpha]_D$ +35 (*c* 2.4 in $CHCl_3$); ν_{max}/cm^{-1} 700, 742, 973, 1097, 1361, 1453, 1493, 1599, 2867, 3027, 3332 and 3430; δ_H (500 MHz, $CDCl_3$) 0.98 (3 H, d, *J* 7.3, 6-CH_3), 1.66 (1 H, br s, OH), 2.00 (1 H, br s, NH), 2.16–2.27 (2 H, m, 3-H_2), 2.44 (1 H, sep, *J* 6.7, 6-H), 2.68 (1 H, m, 2-H), 3.21–3.26 (2 H, m, 1-H_2), 3.33 (1 H, dd, *J*, 10.6 and 5.9, 7-H), 3.57 (1 H, dd, *J* 10.6 and 4.3, 7-H), 4.42 (2 H, s, $PhCH_2$), 4.98 (1 H, s, Ph_2CH), 5.34 (1 H, dt, *J* 15.5 and 7.1, 4-H), 5.44 (1 H, dd, *J* 15.5 and 7.1, 5-H) and 7.18–7.38 (15 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 17.12, 35.09, 37.03, 55.76, 63.55, 64.12, 72.94, 75.17, 125.90, 127.13, 127.19, 127.30, 127.43, 127.51, 127.57, 128.35, 128.55, 128.59, 136.70, 138.57, 143.64 and 144.12; *m*/*z* (CI) 416 (M^+ + 1, 40%) and 167 (100).

Butyl (2*S*,6*S*,*E*)-7-*tert*-butyldimethylsilyloxy-6-(2-trimethylsilylethoxy)methoxy-2-[(*R*)-(1-phenylethyl)amino]hept-4-enoate 108

The general procedure using tin(IV) chloride (481 mg, 1.85 mmol) in DCM (5 mL), the 4,5-bis-alkoxypentenylstannane **106** (1.23 g, 1.93 mmol) in DCM (5 mL) and the imine (***R*)-11** (452 mg, 1.94 mmol) in DCM (5 mL), after 12 h at −45 °C and chromatography using petrol–ether–triethylamine (90 : 9.5 : 0.5) as eluent, gave the *title compound* **108** (772 mg, 72%) as a colourless oil, no other diastereoisomer was detected by ^1H NMR (Found: M^+ + H, 580.3849. $C_{31}H_{58}NO_5Si_2$ requires *M*, 580.3854); $[\alpha]_D$ +62 (*c* 1.18 in $CHCl_3$); ν_{max}/cm^{-1} 667, 700, 777, 838, 938, 970, 1027, 1125, 1251, 1377, 1467, 1735, 2931, 2955 and 3335; δ_H (300 MHz, $CDCl_3$) 0.07 (9 H, s, 3 × CH_3Si), 0.10 (6 H, s, 2 × $SiCH_3$), 0.93 [9 H, s, $SiC(CH_3)_3$], 0.98 (2 H, m, $SiCH_2$), 0.97 (3 H, t, *J* 7.3, CH_3CH_2), 1.38 (3 H, d, *J* 6.4, $PhCHCH_3$), 1.38 (2 H, hex, *J* 7.4, CH_3CH_2), 1.59 (2 H, qn, *J* 7.3, CH_2CH_2O), 1.90 (1 H, br s, NH), 2.36–2.51 (2 H, m, 3-H_2), 3.38 (1 H, t, *J* 6.3, 2-H), 3.52–3.82 (5 H, m, 7-H_2, $PhCHCH_3$ and $SiCH_2CH_2O$), 4.02 (2 H, t, *J* 6.5, CH_2CH_2O), 4.13 (1 H, m, 6-H), 4.70 and 4.75 (each 1 H, d, *J* 6.9, OHCHO), 5.47 (1 H, dd, *J* 15.6 and 7.2, 5-H), 5.72 (1 H, dt, *J* 15.6 and 6.9, 4-H) and 7.26–7.36 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −5.28, −5.22, −1.34, 13.70, 18.07, 18.43, 19.14, 23.18, 25.97, 30.64, 36.25, 56.17, 58.88, 64.49, 65.04, 66.48, 77.11, 92.34, 126.76, 127.12, 128.42, 129.72, 130.66, 145.24 and 174.49; *m*/*z* (CI) 580 (M^+ + 1, 100%).

Butyl (2*S*,6*S*,*E*)- and (2*R*,6*S*,*E*)-7-*tert*-butyldimethylsilyloxy-6-(2-trimethylsilylethoxy)methoxy-2-[(*S*)-(1-phenylethyl)amino]hept-4-enoate 109 and 110

The general procedure using tin(IV) chloride (451 mg, 1.73 mmol) in DCM (5 mL), 4,5-bisalkoxypentenylstannane **106** (1.16 g, 1.82 mmol) in DCM (5 mL) and the imine (***S*)-11** (424 mg, 1.82 mmol) in DCM (5 mL), after 12 h at −45 °C and chromatography using petrol–ether–triethylamine (90 : 9.5 : 0.5) as eluent, gave the *title compounds* **109** and **110** (682 mg, 68%) as a colourless oil, **109** : **110** = 96 : 4 (^1H NMR) (Found: M^+ + H, 580.3843. $C_{31}H_{58}NO_5Si_2$ requires *M*, 580.3854); $[\alpha]_D$ +21 (*c* 0.97 in $CHCl_3$); ν_{max}/cm^{-1} 701, 778, 837, 1027, 1058, 1127, 1180, 1251, 1469, 1734, 2859, 2956 and 3336; δ_H (300 MHz, $CDCl_3$) major isomer 0.06 (9 H, s, 3 × CH_3Si), 0.10 (6 H, s, 2 × CH_3Si), 0.93 [9 H, s, $SiC(CH_3)_3$], 0.97 (2 H, m, $SiCH_2$), 0.99 (3 H, t, *J* 7.3, CH_3CH_2), 1.37 (3 H, d, *J* 6.4, $PhCHCH_3$), 1.41 (2 H, hex, *J* 7.6, CH_3CH_2), 1.65 (2 H, qn, *J* 7.0, CH_2CH_2O), 1.82 (1 H, br s, NH), 2.28–2.47 (2 H, m, 3-H_2), 3.10 (1 H, t, *J* 6.5, 2-H), 3.51–3.81 (5 H, m, 7-H_2, $PhCHCH_3$ and $SiCH_2CH_2O$), 4.07–4.23 (3 H, m, 6-H and CH_2CH_2O), 4.70 and 4.73 (each 1 H, d, *J* 6.9, OHCHO), 5.42 (1 H, dd, *J* 15.5 and 7.3, 5-H), 5.68 (1 H, dt, *J* 15.5 and 7.5, 4-H) and 7.27–7.40 (5 H, m, ArH); minor isomer 3.39 (t, *J* 6.5, 2-H); δ_C (75 MHz, $CDCl_3$) major isomer −5.26, −5.21, −1.34, 13.69, 18.07, 18.44, 19.15, 25.36, 25.98, 30.75, 36.93, 56.60, 58.83, 64.42, 65.03, 66.50, 92.31, 126.91, 127.06, 128.41, 129.92, 130.44, 144.98 and 175.26; *m*/*z* (CI) 580 (M^+ + 1, 100%).

Methyl (2*S*,6*S*,*E*)-7-*tert*-butyldimethylsilyloxy-6-(2-trimethylsilylethoxy)methoxy-2-(2-nitrophenylsulfanyl)-aminohept-4-enoate 111

The general procedure using tin(IV) chloride (1.86 g, 7.14 mmol) in DCM (15 mL), the 4,5-bisalkoxypentenylstannane **106** (4.77 g, 7.50 mmol) in DCM (15 mL) and the imine **29** (1.80 g, 7.49 mmol) in DCM (15 mL), after 12 h at −45 °C and

chromatography using petrol–ether–triethylamine (60 : 39.5 : 0.5) as eluent, gave the *title compound* **111** (3.39 g, 81%) as a yellow oil, no other diastereoisomer was detected by ^{1}H NMR (Found: $M^+ + NH_4$, 604.2900. $C_{26}H_{50}N_3O_7Si_2S$ requires *M*, 604.2908); $[\alpha]_D$ +25.4 (*c* 2.05 in $CHCl_3$); ν_{max}/cm^{-1} 736, 780, 837, 973, 1025, 1100, 1250, 1305, 1338, 1513, 1567, 1593, 1742, 2953 and 3331; δ_H (300 MHz, $CDCl_3$) 0.01 (9 H, s, 3 × CH_3Si), 0.09 (6 H, s, 2 × CH_3Si), 0.91 [9 H, s, $SiC(CH_3)_3$], 0.95 (2 H, t, *J* 8.9, $SiCH_2$), 2.53–2.77 (2 H, m, 3-H_2), 3.45 (1 H, d, *J* 8.8, NH), 3.56–3.79 (5 H, m, 2-H, 7-H_2 and $SiCH_2CH_2O$), 3.81 (3 H, s, CH_3O), 4.14 (1 H, dt, *J* 11.9 and 5.9, 6-H), 4.73 and 4.78 (each 1 H, d, *J* 6.8, OHC*H*O), 5.59 (1 H, dd, *J* 15.5 and 7.0, 5-H), 5.73 (1 H, dt, *J* 15.5 and 7.1, 4-H), 7.29 (1 H, ddd, *J* 8.1, 8.1 and 1.1, ArH), 7.68 (1 H, ddd, *J* 7.9, 7.9 and 1.1, ArH), 8.10 (1 H, dd, *J* 7.9 and 1.0, ArH) and 8.30 (1 H, dd, *J* 8.0 and 1.0, ArH); δ_C (75 MHz, $CDCl_3$) −5.26, −5.21, −1.41, 18.07, 18.43, 25.82, 25.95, 36.48, 52.39, 63.46, 65.22, 66.27, 92.70, 124.60, 124.77, 125.78, 127.95, 132.67, 133.88, 142.56, 144.98 and 173.48; *m*/*z* (CI) 604 (M^+ + 18, 4%), 587 (M^+ + 1, 2), 439 (50) and 147 (100).

Methyl (2*S*,6*S*,*E*)-2-acetamido-7-*tert*-butyldimethylsilyloxy-6-(2-(trimethylsilyl)ethoxy)methoxyhept-4-enoate 112

Triethylamine (1.07 mL, 7.68 mmol), acetic anhydride (362 μL, 3.83 mmol) and DMAP (3 mg, 25 μmol) were added to the 2-(arylsulfanyl)aminoheptenoate **111** (750 mg, 1.28 mmol) in chloroform (15 mL) and this mixture was heated under reflux for 16 h. After cooling to ambient temperature, water (20 mL) was added and, after 10 min, by more DCM. The organic layer was washed with saturated aqueous sodium hydrogen carbonate and dried ($MgSO_4$). The solution was absorbed on to silica and the resulting powder applied to a column of silica gel. Elution with hexane–ethyl acetate (3 : 2) gave the *title compound* **112** (450 mg, 74%) as a pale yellow oil (Found: M^+ + H, 476.2862. $C_{22}H_{46}NO_6Si_2$ requires *M*, 476.2864); ν_{max}/cm^{-1} 775, 834, 1023, 1102, 1249, 1372, 1437, 1536, 1658, 1746, 2858, 2952 and 3293; δ_H (300 MHz, $CDCl_3$) 0.05 (9 H, s, 3 × CH_3Si), 0.10 (6 H, s, 2 × CH_3Si), 0.92 [9 H, s, $SiC(CH_3)_3$], 0.96 (2 H, t, *J* 7.9, $SiCH_2$), 2.05 (3 H, s, CH_3CO), 2.50–2.67 (2 H, m, 3-H_2), 3.52–3.89 (4 H, m, 7-H_2 and $SiCH_2CH_2O$), 3.78 (3 H, s, CH_3O), 4.09 (1 H, m, 6-H), 4.67–4.75 (3 H, m, 2-H and OCH_2O), 5.51 (1 H, dd, *J* 15.5 and 6.9, 5-H), 5.60 (1 H, dt, *J* 15.5 and 6.7, 4-H) and 6.14 (1 H, d, *J* 8.7, NH); δ_C (75 MHz, $CDCl_3$) −5.27, −1.39, 18.07, 18.42, 23.12, 25.94, 35.14, 51.76, 52.40, 65.09, 66.29, 77.32, 92.43, 127.61, 132.52, 169.67 and 172.22; *m*/*z* (CI) 493 (M^+ + 18, 5%), 476 (M^+ + 1, 4), 418 (10) and 328 (100).

The general procedure using the 2-acetamidoheptenoate **112** (250 mg, 0.525 μmol), ozone, methyl sulfide (116 μL, 1.58 mmol) and sodium borohydride (80 mg, 2.11 mmol) gave an alcohol that was cyclised using glacial acetic acid in chloroform to give, after chromatography using chloroform–triethylamine (99.5 : 0.5) as eluent, the (*S*)-acetamidolactone **113** (45 mg, 60%) (Found C, 50.45; H, 6.5; N, 9.5. $C_6H_9NO_3$ requires C, 50.35; H, 6.5; N, 9.8); $[\alpha]_D$ +14.4 (*c* 1.1 in CH_2Cl_2), $[\alpha]_D$ −63 (*c* 1.6 in DMF) [lit.[21] −54.7 (in DMF)]; ν_{max}/cm^{-1} 1034, 1179, 1344, 1381, 1428, 1538, 1638, 1783 and 3305; δ_H (300 MHz, $CDCl_3$) 2.09 (3 H, s, CH_3CO), 2.20 and 2.82 (each 1 H, m, 4-H), 4.27–4.36 (1 H, m, 5-H), 4.49 (1 H, t, *J* 9.0, 3-H), 4.59–4.69 (1 H, m, 5-H) and 6.50 (1 H, br s, NH); δ_C (75 MHz, $CDCl_3$) 22.84, 30.27, 49.22, 66.14, 170.79 and 175.76; *m*/*z* (CI) 161 (M^+ + 18, 95%) and 144 (M^+ + 1, 100).

Methyl (2*S*,6*S*,*E*)-2-(diphenylmethyl)amino-7-*tert*-butyldimethylsilyloxy-6-(2-trimethylsilylethoxy)methoxyhept-4-enoate 115

The general procedure using tin(IV) chloride (313 mg, 1.20 mmol) in DCM (5 mL), the 4,5-bis-alkoxypentenylstannane **106** (802 mg, 1.26 mmol) in DCM (5 mL) and the imine **114** (320 mg, 1.26 mmol) in DCM (5 mL) after chromatography using petrol–ether–triethylamine (90 : 9.5 : 0.5) as eluent gave the *title compound* **115** (519 mg, 72%) as a colourless oil, no other diastereoisomer was detected by ^{1}H NMR (Found: M^+ + H, 600.3547. $C_{33}H_{54}NO_5Si_2$ requires *M*, 600.3541); $[\alpha]_D$ +31 (*c* 0.45 in $CHCl_3$); ν_{max}/cm^{-1} 702, 778, 836, 1027, 1056, 1106, 1127, 1250, 1453, 1738, 2928, 2952 and 3332; δ_H (300 MHz, $CDCl_3$) 0.06 (9 H, s, 3 × CH_3Si), 0.10 (6 H, s, 2 × CH_3Si), 0.91–0.99 [11 H, m, $SiC(CH_3)_3$ and $SiCH_2$], 2.18 (1 H, br s, NH), 2.40–2.50 (2 H, m, 3-H_2), 3.33 (1 H, t, *J* 6.3, 2-H), 3.52–3.81 (4 H, m, 7-H_2 and $SiCH_2CH_2O$), 3.74 (3 H, s, CH_3O), 4.14 (1 H, m, 6-H), 4.68 and 4.73 (each 1 H, d, *J* 6.8, OHC*H*O), 4.84 (1 H, s, Ph_2CH), 5.45 (1 H, dd, *J* 15.5 and 7.5, 5-H), 5.76 (1 H, dt, *J* 15.5 and 7.9, 4-H) and 7.20–7.48 (10 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −5.25, −5.20, −1.32, 18.07, 18.46, 25.98, 36.82, 51.67, 59.03, 65.06, 65.38, 66.49, 92.22, 127.23, 127.30, 127.56, 128.53, 128.90, 129.80, 130.63, 142.67, 144.14 and 175.26; *m*/*z* (CI) 600 (M^+ + 1, 70%) and 90 (100).

Methyl (2*S*,6*S*)-2-(diphenylmethyl)amino-7-(*tert*-butyldimethylsilyloxy)-6-(2-trimethylsilylethoxy)methoxyheptanoate 116

The general procedure using heptenoate **115** (445 mg, 0.742 μmol), toluene 4-sulfonylhydrazine (1.38 g, 7.41 mmol) and anhydrous sodium acetate (608 mg, 7.41 mmol) after chromatography using hexane–ether–triethylamine (90 : 9.5 : 0.5) as eluent gave the *title compound* **116** (402 mg, 90%) as a colourless oil (Found: M^+ + H, 602.3696. $C_{33}H_{56}NO_5Si_2$ requires *M*, 602.3697); $[\alpha]_D$ −21 (*c* 2.0 in $CHCl_3$); ν_{max}/cm^{-1} 701, 777, 838, 1030, 1104, 1251, 1462, 1737, 2951 and 3336; δ_H (300 MHz, $CDCl_3$) 0.05 (9 H, s, 3 × CH_3Si), 0.10 (6 H, s, 2 × CH_3Si), 0.88–0.99 [11 H, m, $SiC(CH_3)_3$ and $SiCH_2$], 1.48–1.73 (6 H, m, 3-H_2, 4-H_2 and 5-H_2), 2.11 (1 H, br s, NH), 3.24 (1 H, t, *J* 6.3, 2-H), 3.56–3.70 (5 H, m, 6-H, 7-H_2 and $SiCH_2CH_2O$), 3.74 (3 H, s, CH_3O), 4.73 (1 H, d, *J* 7.1, OHC*H*O), 4.80 (1 H, s, Ph_2CH), 4.83 (1 H, d, *J* 7.1, OHC*H*O) and 7.20–7.50 (10 H, m, ArH); δ_C (75 MHz, $CDCl_3$) −5.35, −5.32, −1.37, 18.08, 18.35, 21.73, 25.96, 31.58, 34.12, 51.67, 59.07, 65.12, 65.57, 65.70, 77.90, 94.58, 127.18, 127.32, 127.60, 128.50, 128.52, 142.78, 144.36 and 176.24; *m*/*z* (CI) 602 (M^+ + 1, 100%).

Methyl (2*S*,6*S*)-2-(diphenylmethyl)amino-6,7-dihydroxyheptanoate 117

The α-amino ester **116** (301 mg, 0.500 μmol) was dissolved in saturated hydrogen chloride in methanol (5 mL) and the solution

stirred at ambient temperature for 2 h. After concentration under reduced pressure, the residue was dissolved in chloroform, absorbed on to silica and the resulting powder applied to a column of silica gel. Elution with hexane–ethyl acetate–methanol (50 : 48 : 2) as eluent gave the *title compound* **117** (179 mg, 100%) as a colourless oil (Found: M^+ + H, 358.2010. $C_{21}H_{28}NO_4$ requires *M*, 358.2018); $[\alpha]_D$ −23.5 (*c* 1.7 in $CHCl_3$); ν_{max}/cm^{-1} 703, 747, 1029, 1058, 1137, 1171, 1202, 1436, 1453, 1492, 1732, 2864, 2946 and 3399; δ_H (300 MHz, $CDCl_3$) 1.36–1.46, 1.51–1.63 and 1.64–1.75 (each 2 H, m), 2.30 (3 H, br s, NH and 2 × OH), 3.25 (1 H, t, *J* 6.5, 2-H), 3.44 (1 H, dd, *J* 11.1 and 7.4, 7-H), 3.61–3.76 (2 H, m, 6-H and 7-H), 3.76 (3 H, s, CH_3O), 4.81 (1 H, s, Ph_2CH) and 7.20–7.50 (10 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 21.78, 32.71, 33.60, 51.81, 58.96, 65.63, 66.74, 71.87, 127.30, 127.66, 128.55, 128.57, 142.62, 144.16 and 176.20; *m*/*z* (CI) 358 (M^+ + 1, 100%).

Methyl (2*S*,6*S*)-6,7-dihydroxy-2-[(1,1-dimethyl)ethoxycarbonyl]-aminoheptanoate 118

The general procedure for transfer hydrogenation using the heptanoate **117** (774 mg, 2.17 mmol) gave an oil that was dissolved in DCM (7.5 mL) and triethylamine (2.5 mL, 17.94 mmol) and 2-(*tert*-butoxycarbonyloxyimino)-2-phenylacetonitrile (587 mg, 2.38 mmol) were added. The mixture was heated under reflux for 3 h and cooled to ambient temperature. After concentration under reduced pressure, the residue was dissolved in chloroform and the solution washed with saturated aqueous sodium hydrogen carbonate, water and brine then dried ($MgSO_4$). The solution was absorbed onto silica and the ensuing powder applied to a column of silica gel. Elution with chloroform–methanol (99 : 1 to 99 : 5) as eluent gave the *title compound* **118** (442 mg, 70%) as a colourless oil (Found: M^+ + H, 292.1769. $C_{13}H_{26}NO_6$ requires *M*, 292.1760); $[\alpha]_D$ +6.14 (*c* 2.2 in $CHCl_3$); ν_{max}/cm^{-1} 1054, 1167, 1251, 1367, 1440, 1456, 1522, 1696, 1740, 2949 and 3374; δ_H (300 MHz, $CDCl_3$) 1.46 [9 H, s, $C(CH_3)_3$], 1.46–1.85 (6 H, m, 3-H_2, 4-H_2 and 5-H_2), 2.70 (2 H, br s, 2 × OH), 3.46 (1 H, dd, *J* 11.4 and 7.3, 7-H), 3.65 (1 H, dd, *J* 11.4 and 8.0, 7-H), 3.75 (1 H, m, 6-H), 3.78 (3 H, s, CH_3O), 4.33 (1 H, m, 2-H) and 5.21 (1 H, br d, *J* 8.1, NH); δ_C (75 MHz, $CDCl_3$) 21.29, 28.33, 32.31, 32.81, 52.30, 53.11, 66.74, 71.77, 80.11, 155.62 and 173.34; *m*/*z* (CI) 292 (M^+ + 1, 2%), 236 (40) and 192 (100).

Methyl (2*S*,6*S*)-6-hydroxy-2-[(1,1-dimethyl)ethoxycarbonyl]-amino-7-[(2,4,6-trimethylphenyl)sulfonyloxy]heptanoate 119

2-Mesitylenesulfonyl chloride (206 mg, 0.942 µmol) in pyridine (5 mL) cooled to 0 °C) was added to the diol **118** (250 mg, 0.858 µmol) in pyridine (1 mL) and the solution stirred at 0 °C for 16 h. The reaction mixture was concentrated under reduced pressure and the residue suspended in water and extracted into chloroform. The organic layer was washed with aqueous hydrogen chloride (1 M) and water then dried ($MgSO_4$). After concentration under reduced pressure, the ensuing oil was applied to a column of silica gel. Elution with chloroform–methanol (99 : 1) as eluent gave the *title compound* **119** (337 mg, 83%) as a colourless oil (Found: M^+ + H, 474.2161. $C_{22}H_{36}NO_8S$ requires *M*, 474.2162); $[\alpha]_D$ +6.6 (*c* +1.9 in $CHCl_3$); ν_{max}/cm^{-1} 816, 972, 1173, 1250, 1355, 1455, 1514, 1712, 1742, 2950 and 3430; δ_H (300 MHz, $CDCl_3$) 1.48 [9 H, s, $C(CH_3)_3$], 1.48–1.87 (6 H, m, 3-H_2, 4-H_2 and 5-H_2), 2.33 (3 H, s, $PhCH_3$), 2.35 (1 H, br, s OH), 2.68 (6 H, s, 2 × $PhCH_3$), 3.78 (3 H, s, CH_3O), 3.84–3.98 (3 H, m, 6-H and 7-H_2), 4.40 (1 H, m, 2-H), 5.10 (1 H, d, *J* 8.6, NH) and 7.01 (2 H, s, ArH); δ_C (75 MHz, $CDCl_3$) 21.04, 22.60, 28.32, 32.09, 32.70, 52.32, 52.95, 69.18, 72.86, 80.08, 130.35, 131.83, 139.96, 143.52, 155.53 and 173.14; *m*/*z* (CI) 491 (M^+ + 18, 2%), 474 (M^+ + 1, 20) and 374 (100).

Methyl (2*S*,6*S*)-6,7-epoxy-2-[(1,1-dimethyl)ethoxycarbonyl]-aminoheptanoate 120

Potassium *tert*-butoxide (62 mg, 0.552 µmol) was added to the mesitylate **119** (250 mg, 0.528 µmol) in THF (5 mL) at −78 °C and the mixture stirred at −78 °C for 5 min. Methanol (500 µL) and water (500 µL) were added and the mixture was allowed to warm to ambient temperature. Ether (10 mL) was added and the solution absorbed on to silica. The resulting powder was applied to a column of silica gel. Elution using chloroform gave the *title compound* **120** (120 mg, 83%) as a colourless oil (Found: M^+ 273.1581. $C_{13}H_{23}NO_5$ requires *M*, 273.1576); $[\alpha]_D$ +3.79 (*c* 0.95 in $CHCl_3$); ν_{max}/cm^{-1} 1166, 1212, 1252, 1366, 1454, 1517, 1714, 1745 and 2976; δ_H (300 MHz, $CDCl_3$) 1.48 [9 H, s, $C(CH_3)_3$], 1.49–1.93 (6 H, m, 3-H_2, 4-H_2 and 5-H_2), 2.50 (1 H, dd, *J* 5.1 and 2.9, 7-H), 2.78 (1 H, dd, *J* 5.1 and 4.7, 7-H), 2.93 (1 H, m, 6-H), 3.76 (3 H, s, CH_3O), 4.35 (1 H, m, 2-H) and 5.08 (1 H, d, *J* 7.6, NH); δ_C (75 MHz, $CDCl_3$) 21.97, 28.32, 31.88, 32.53, 46.89, 51.84, 52.26, 53.35, 79.95, 155.33 and 173.17; *m*/*z* (CI) 291 (M^+ + 18, 10%), 274 (M^+ + 1, 30) and 114 (100).

Methyl (2*S*,6*R*)-6-(hydroxymethyl)piperidinyl-2-carboxylate 121

Trifluoroacetic acid (1 mL) was added to the epoxide **120** (100 mg, 0.366 µmol) in chloroform (1 mL) and the solution was stirred at ambient temperature for 2 h. After concentration under a high vacuum (0.5 mm Hg), the residue was dissolved in chloroform and absorbed onto silica. The resulting powder was applied to a column of silica gel. Elution with chloroform then chloroform–methanol (95 : 5) gave the *title compound* **121** (43 mg, 68%) as a colourless oil (Found: M^+ + H, 174.1132. $C_8H_{16}NO_3$ requires *M*, 174.1130); $[\alpha]_D$ −14 (*c* 1.1 in $CHCl_3$); ν_{max}/cm^{-1} 1046, 1102, 1213, 1295, 1439, 1739, 2934 and 3385; δ_H (500 MHz, $CDCl_3$) 1.13 (1 H, m), 1.33–1.42 (2 H, m), 1.52, 1.87 and 1.99 (each 1 H, m), 2.27 (2 H, br s, NH and OH), 2.69 (1 H, m, 6-H), 3.34 (1 H, dd, *J* 10.8 and 2.6, 2-H), 3.44 (1 H, dd, *J* 10.8 and 7.7, 6-CH), 3.61 (1 H, dd, *J* 10.8 and 3.4, 6-CH) and 3.70 (3 H, s, CH_3O); δ_C (75 MHz, $CDCl_3$) 24.01, 27.66, 29.26, 51.97, 57.55, 58.78, 66.71 and 173.72; *m*/*z* (CI) 174 (M^+ + 1, 100%) and 142 (55).

Butyl (2*S*,7*S*,4*E*)- and (2*R*,7*S*,4*E*)-7-methoxy-2-[(*S*)-(1-phenylethyl)amino]oct-4-enoates 126 and 127

The general procedure using the (*S*)-5-methoxyhexenylstannane (***S*)-123** (63 mg, 0.155 mmol), tin(IV) bromide in DCM (1 M, 155 µL, 0.155 mmol) and the (*S*)-imine (***S*)-11** (35 mg,

0.150 mmol) after 8 h at −50 °C and chromatography using DCM–ether–triethylamine (90 : 9.5 : 0.5) as eluent gave the *title compounds* **126** and **127** (33 mg, 68%) as a colourless oil, **126** : **127** = 16 : 84 (^{1}H NMR). Samples of each were obtained as colourless oils by preparative HPLC using hexane–ethyl acetate (2 : 1) as eluent: (2*R*)-epimer **127** (less polar, 86% of the mixture), (Found: M^+ + H, 348.2537. $C_{21}H_{34}O_3N$ requires *M*, 348.2539); ν_{max}/cm^{-1} 701, 1094, 1136, 1181, 1453, 1733, 2964 and 3395; δ_H (500 MHz, $CDCl_3$) 0.89 (3 H, t, *J* 7.5, C*H*$_3$CH$_2$), 1.09 (3 H, d, *J* 6.5, 8-H$_3$), 1.31 (2 H, hex, *J* 7.5, CH$_3$C*H*$_2$), 1.32 (3 H, d, *J* 6.5, NCHC*H*$_3$), 1.52 (2 H, qn, *J* 7.5, C*H*$_2$CH$_2$O), 1.87 (1 H, br s, NH), 2.09 and 2.26 (each 1 H, dt, *J* 14 and 7, 6-H), 2.31 (2 H, t, *J* 7, 3-H$_2$), 3.26–3.20 (2 H, m, 2-H and 7-H), 3.28 (3 H, s, 7-OCH$_3$), 3.76 (1 H, q, *J* 6.5, NC*H*CH$_3$), 3.94 (2 H, t, *J* 7.5, CH$_2$C*H*$_2$O), 5.39 (1 H, dt, *J* 15 and 7.5, 5-H), 5.48 (1 H, dt, *J* 15 and 7.5, 4-H) and 7.19–7.29 (5 H, m, ArH); δ_C (125 MHz, $CDCl_3$) 13.65, 18.78, 19.07, 23.09, 30.57, 36.22, 39.13, 55.94, 58.87, 64.35, 76.50, 126.75, 126.75, 127.27, 128.33, 129.94, 145.09 and 174.55; *m*/*z* (CI) 348 (M^+ + 1, 100%): (2*S*)-epimer **126** (more polar, 14% of the mixture) (Found: M^+ + H, 348.2545. $C_{21}H_{34}O_3N$ requires *M*, 348.2539); ν_{max}/cm^{-1} 701, 1094, 1135, 1181, 1372, 1453, 1732, 2962 and 3330; δ_H (500 MHz, $CDCl_3$) 0.91 (3 H, t, *J* 7.5, C*H*$_3$CH$_2$), 1.09 (3 H, d, *J* 6.5, 8-H$_3$), 1.31 (3 H, d, *J* 6.5, NCHC*H*$_3$), 1.35 (2 H, hex, *J* 7.5, CH$_3$C*H*$_2$), 1.58 (2 H, qn, *J* 7.5, C*H*$_2$CH$_2$O), 1.77 (1 H, br s, NH), 2.09 and 2.22 (each 1 H, dt, *J* 14 and 7, 6-H), 2.27 (2 H, t, *J* 7, 3-H$_2$), 3.03 (1 H, t, *J* 6.5, 2-H), 3.30 (1 H, m, 7-H), 3.29 (3 H, s, 7-OCH$_3$), 3.69 (1 H, q, *J* 6.5, NC*H*CH$_3$), 4.09 (2 H, t, *J* 7.5, CH$_2$C*H*$_2$O), 5.34 (1 H, dt, *J* 15 and 7.5, 5-H), 5.44 (1 H, dt, *J* 15 and 7.5, 4-H), 7.21 (1 H, m, ArH) and 7.26–7.29 (4 H, m, ArH); δ_C (125 MHz, $CDCl_3$) 13.65, 18.78, 19.09, 25.24, 36.67, 37.05, 39.04, 55.92, 55.95, 58.79, 64.26, 76.50, 126.83, 126.95, 127.55, 128.30, 129.62, 144.95 and 175.28; *m*/*z* (CI) 348 (M^++1, 100%). Further elution with DCM–ether–triethylamine (90 : 9.5 : 0.5) gave butyl (2*SR*,7*S*,4*ZE*)-2-hydroxy-7-methoxy-oct-4-enoate (10 mg, 18%).

n-Butyl (2*S*,7*S*,4*E*)- and (2*R*,7*S*,4*E*)-7-methoxy-2-[(*R*)-(1-phenylethyl)amino]oct-4-enoate 128 and 129

The general procedure using the (*S*)-5-methoxyhexenylstannane (***S*)-123** (59 mg, 0.145 mmol) in DCM (1 mL), the (*R*)-imine (***R*)-11** (33 mg, 0.141 mmol) in DCM (0.5 mL) and tin(IV) bromide in DCM (1 M, 145 μL, 0.145 mmol) at −50 °C for 8 h and chromatography using DCM–ether–triethylamine (90 : 9.5 : 0.5) as the eluent gave the *title compounds* **128** and **129** (35 mg, 72%) as a colourless oil, **128** : **129** = 92 : 8 (^{1}H NMR) together with butyl (2*SR*,7*S*,4*ZE*)-2-hydroxy-7-methoxy-oct-4-enoate (5 mg, 11%) as a colourless oil. Samples of each title compound were obtained as colourless oils by preparative HPLC using hexane–ethyl acetate (2 : 1) as the eluent: (2*S*)-epimer **128** (less polar, 92% of the mixture), $[\alpha]_D$ +12 (*c* 1.61 in DCM) (Found: M^+ + H, 348.2544. $C_{21}H_{34}O_3N$ requires *M*, 348.2539); ν_{max}/cm^{-1} 701, 969, 1183, 1372, 1454, 1702 and 2964; δ_H (500 MHz, $CDCl_3$) 0.89 (3 H, t, *J* 7.5, C*H*$_3$CH$_2$), 1.08 (3 H, d, *J* 6.5, 8-H$_3$), 1.31 (2 H, hex, *J* 7.5, CH$_3$C*H*$_2$), 1.32 (3 H, d, *J* 6.5, NCHC*H*$_3$), 1.52 (2 H, qn, *J* 7.5, C*H*$_2$CH$_2$O), 1.91 (1 H, br s, NH), 2.10 and 2.22 (each 1 H, dt, *J* 14 and 7, 6-H), 2.34 (2 H, t, *J* 6.5, 3-H$_2$), 3.28 (1 H, m, 7-H), 3.28 (3 H, s, 7-OC*H*$_3$), 3.31 (1 H, t, *J* 6.5, 2-H), 3.76 (1 H, q, *J* 6.5, NC*H* CH$_3$), 3.95 (2 H, t, *J* 7.5, CH$_2$C*H*$_2$O), 5.40 (1 H, dt, *J* 15.5 and 7.5, 5-H), 5.48 (1 H, dt, *J* 15.5 and 7.5, 4-H) and 7.19–7.28 (5 H, m, ArH); δ_C (125 MHz, $CDCl_3$) 13.65, 18.76, 19.07, 23.08, 30.57, 36.22, 39.11, 55.91, 56.05, 58.89, 64.35, 76.50, 126.77, 127.06, 127.27, 128.33, 129.94, 145.05 and 174.54; *m*/*z* (CI) 348 (M^+ + 1, 100%); (2*R*)-epimer **129** (more polar, 8% of the mixture), $[\alpha]_D$ +54 (*c* 0.36 in DCM) (Found: M^+ + H, 348.2535. $C_{21}H_{34}O_3N$ requires *M*, 348.2539); ν_{max}/cm^{-1} 701, 1183, 1393, 1453 and 1731 and 3331; δ_H (500 MHz, $CDCl_3$) 0.91 (3 H, t, *J* 7.5, C*H*$_3$CH$_2$), 1.08 (3 H, d, *J* 6.5, 8-H$_3$), 1.30 (3 H, d, *J* 6.5, NCHC*H*$_3$), 1.35 (2 H, hex, *J* 7.5, CH$_3$C*H*$_2$), 1.49–1.56 (3 H, m, C*H*$_2$CH$_2$O and NH), 2.08 (1 H, dt, *J* 14 and 7, 6-H), 2.22 (1 H, dt, *J* 14 and 7, 6-H), 2.26 (2 H, dd, *J* 7 and 7, 3-H$_2$), 3.02 (1 H, t, *J* 6.5, 2-H), 3.28 (1 H, m, 7-H), 3.29 (3 H, s, 7-OCH$_3$), 3.68 (1 H, q, *J* 6.5, NC*H*CH$_3$), 4.08 (2 H, t, *J* 7.5, CH$_2$C*H*$_2$O), 5.35 (1 H, dt, *J* 15.5 and 7.5, 5-H), 5.43 (1 H, dt, *J* 15.5 and 7.5, 4-H) and 7.20–7.29 (5 H, m, ArH); *m*/*z* (CI) 348 (M^+ + 1, 100%).

Butyl (2*S*,7*S*,4*E*)- and (2*R*,7*S*,4*E*)-2-(diphenylmethyl)amino-7-methoxyoct-4-enoate 139 and 140

The general procedure using the (*S*)-methoxyhexenylstannane (***S*)-123** (192 mg, 0.474 mmol) in DCM (6 mL), the imine **32** (136 mg, 0.460 mmol) in DCM (2 mL) and tin(IV) bromide in DCM (1 M, 474 μL, 0.474 mmol) after 24 h at −50 °C and chromatography using hexane–ethyl acetate–triethylamine (60 : 39 : 1) as eluent gave a mixture of the *title compounds* **139** and **140** (116 mg, 62%) as a colourless oil, $[\alpha]_D$ −21.3 (*c* 0.84 in DCM) (Found: M^+ + H, 410.2689. $C_{26}H_{36}O_3N$ requires *M*, 410.2695); ν_{max}/cm^{-1} 702, 745, 969, 1027, 1095, 1138, 1183, 1276, 1345, 1453, 1731, 2962 and 3330; δ_H (300 MHz, $CDCl_3$) 0.98 (3 H, t, *J* 7.5, C*H*$_3$CH$_2$), 1.15 (3 H, d, *J* 6.5, 8-H$_3$), 1.41 (2 H, m, CH$_3$C*H*$_2$), 1.64 (2 H, m, C*H*$_2$CH$_2$O), 2.19 (1 H, br s, NH), 2.24 (2 H, m, 6-H$_2$), 2.44 (2 H, t, *J* 6.5, 3-H$_2$), 3.27–3.40 (2 H, m, 7-H and 2-H), 3.34 (3 H, s, 7-OCH$_3$), 4.20 (2 H, t, *J* 7.5, CH$_2$C*H*$_2$O), 4.86 (1 H, s, NCHPh$_2$), 5.55 (1 H, dt, *J* 15 and 7.5, 5-H), 5.60 (1 H, dt, *J* 15 and 7.5, 4-H) and 7.20–7.90 (10 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 13.64, 18.77, 19.09, 30.67, 36.89, 39.11, 55.91, 59.03, 64.34, 65.26, 76.50, 127.06, 127.27, 127.46, 127.52, 128.37, 128.40, 129.78, 142.78, 144.20 and 174.87; *m*/*z* (CI) 410 (M^+ + 1, 100%), 348 (5), 182 (5) and 167 (50).

Butyl (2*S*,7*S*)- and (2*R*,7*S*)-2-amino-7-methoxyoctanoate 141 and 144

10% Pd/C (143 mg, 0.1341 mmol) and ammonium formate (51 mg, 0.805 mmol) were added to the (diphenylmethyl)amino-octenoates **139** and **140** (110 mg, 0.268 mmol) in dry methanol (7 mL) at room temperature and the mixture stirred for 1 h then filtered and the residue washed with methanol. The organic solvents were concentrated under reduced pressure and the residue was dissolved in DCM and washed with water. The aqueous phase was extracted with DCM (5 × 10 mL) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give the *title compounds* **141** and **144** (61 mg, 92%)

as a colourless oil, $[\alpha]_D$ +1.7 (*c* 1.5 in DCM) (Found: M^+ + H, 246.2071. $C_{13}H_{28}O_3N$ requires *M*, 246.2069); ν_{max}/cm^{-1} 724, 1090, 1179, 1375, 1464, 1618, 1734, 2934 and 3307; δ_H (300 MHz, $CDCl_3$) 0.98 (3 H, t, *J* 7.5, CH_3CH_2), 1.17 (3 H, d, *J* 6.5, 8-H_3), 1.38–1.47 (8 H, m, 4-H_2, 5-H_2, CH_3CH_2 and NH_2), 1.53–1.76 (4 H, m, 3-H_2 and 6-H_2), 1.67 (2 H, hex, *J* 7.5, CH_2CH_2O), 3.29 (1 H, m, 7-H), 3.34 (3 H, s, 7-OCH_3), 3.50 (1 H, m, 2-H) and 4.15 (2 H, m, CH_2CH_2O); δ_C (75 MHz, $CDCl_3$) 13.60, 18.91, 19.05, 25.14, 25.69, 30.59, 36.08, 55.87, 64.59, 76.51 and 164.90; *m*/*z* (CI) 247 (M^+ + 2, 14%), 246 (M^+ + 1, 100) and 144 (6).

Butyl (2*S*,7*S*,4*E*)- and (2*R*,7*S*,4*E*)-7-methoxy-2-[(*R*)-2-methoxy-2-phenyl-3,3,3-trifluoropropanoyl]amino-octanoates 142 and 145

The procedure outlined above using (*S*)-Mosher's acid chloride (13 μL, 66 μmol), a mixture of the amino-octanoates **141** and **144** (13 mg, 55 μmol), triethylamine (39 μL, 0.273 mmol) and DMAP (5 mg), after chromatography eluting with petrol–ether (85 : 15), gave the *title compounds* **142** and **145** (19 mg, 76%), as an oil, **142** : **145** = 70 : 30 (^{1}H NMR). Preparative HPLC using hexane–ethyl acetate (90 : 10) as eluent gave the less polar, minor (2*R*)-isomer **145** as a colourless oil, $[\alpha]_D$ +5.5 (*c* 0.51 in DCM) (Found: M^+ + H, 462.2476. $C_{23}H_{35}O_5NF_3$ requires *M*, 462.2467); ν_{max}/cm^{-1} 719, 1104, 1167, 1271, 1513, 1696, 1740, 2934 and 3349; δ_H (300 MHz, $CDCl_3$) 0.97 (3 H, t, *J* 7.5, CH_3CH_2), 1.13 (3 H, d, *J* 6.5, 8-H_3), 1.16–1.38 (6 H, m, 4-H_2, 5-H_2 and 6-H_2), 1.41 (2 H, hex, *J* 7.5, CH_3CH_2), 1.62–1.74 (3 H, m, 3-H and CH_2CH_2O), 1.91 (1 H, m, 3-H), 3.25 (1 H, m, 7-H), 3.32 (3 H, s, 7-OCH_3), 3.58 (3 H, d, *J* 1.5, CH_3O), 4.18 (2 H, m, CH_2CH_2O), 4.69 (1 H, dt, *J* 8.5 and 7.5, 2-H), 7.12 (1 H, d, *J* 8.5, NH), 7.41–7.44 (3 H, m, ArH) and 7.58–7.68 (2 H, m, ArH); *m*/*z* (CI) 479 (M^+ + 18, 14%), 463 (M^+ + 2, 22) and 462 (M^+ + 1, 100); δ_F-70.3; followed by the more polar, major (2*S*)-epimer **142** as a colourless oil, $[\alpha]_D$ −5.5 (*c* 1.04 in DCM) (Found: M^+ + H, 462.2463. $C_{23}H_{35}O_5NF_3$ requires *M*, 462.2467); ν_{max}/cm^{-1} 718, 1104, 1167, 1271, 1513, 1696, 1740 and 3349; δ_H (300 MHz, $CDCl_3$) 0.97 (3 H, t, *J* 7.5, CH_3CH_2), 1.16 (3 H, d, *J* 6.5, 8-H_3), 1.34–1.51 (8 H, m, 4-H_2, 5-H_2 and $CH_3CH_2CH_2$), 1.66 (2 H, m, 6-H_2), 1.79 and 1.99 (each 1 H, m, 3-H), 3.31 (1 H, m, 7-H), 3.34 (3 H, s, 7-OCH_3), 3.40 (3 H, d, *J* 1, CH_3O), 4.18 (2 H, m, CH_2CH_2O), 4.67 (1 H, dt, *J* 8.5 and 7.5, 2-H), 7.43–7.45 (4 H, m, ArH and NH) and 7.58 (2 H, dd, *J* 7.5 and 3.5, ArH); δ_C (75 MHz, $CDCl_3$) 13.57, 18.86, 18.96, 24.83, 25.22, 30.44, 32.20, 35.95, 52.14, 54.78, 55.86, 65.32, 76.44, 127.97, 128.52, 129.44, 131.75, 166.00 and 171.94; *m*/*z* (CI) 479 (M^+ + 18, 20%), 463 (M^+ + 2, 22) and 462 (M^+ + 1, 100).

Butyl (2*S*,7*S*,4*E*)- and (2*R*,7*S*,4*E*)-7-methoxy-2-[(*S*)-2-methoxy-2-phenyl-3,3,3-trifluoropropanoyl]amino-octanoates 143 and 146

The procedure outlined above using (*R*)-Mosher's acid chloride (13 μL, 63 μmol), a mixture of the amino-octanoates **141** and **144** (14 mg, 57 μmol), triethylamine (42 μL, 0.287 mmol) and DMAP (5 mg) after chromatography using petrol–ether (85 : 15) as eluent gave the *title compounds* **143** and **146** (20 mg, 75%) as a pale yellow oil, **143** : **146** = 70 : 30 (^{1}H NMR). Preparative HPLC using hexane–ethyl acetate (90 : 10) as the eluent gave the less polar, major (2*S*)-epimer **143** as a colourless oil, $[\alpha]_D$ −18.4 (*c* 1.13 in DCM) (Found: M^+ + H, 462.2464. $C_{23}H_{35}O_5NF_3$ requires *M*, 462.2467); ν_{max}/cm^{-1}) 734, 1104, 1167, 1270, 1512, 1697, 1740, 2934 and 3357; δ_H (300 MHz, $CDCl_3$) 0.97 (3 H, t, *J* 7.5, CH_3CH_2), 1.12 (3 H, d, *J* 6.5, 8-H_3), 1.18–1.35 (6 H, m, 4-H_2, 5-H_2 and 6-H_2), 1.42 (2 H, hex, *J* 7.5, CH_3CH_2), 1.62–1.71 (3 H, m, 3-H and CH_2CH_2O), 1.92 (1 H, m, 3-H), 3.24 (1 H, m, 7-H), 3.30 (3 H, s, 7-OCH_3), 3.58 (3 H, d, *J* 1.5, CH_3O), 4.14 (2 H, m, CH_2CH_2O), 4.68 (1 H, dt, *J* 8 and 7.5, 2-H), 7.11 (1 H, d, *J* 8, NH), 7.41–7.44 (3 H, m, ArH) and 7.56–7.64 (2 H, m, ArH); δ_C 13.53, 18.84, 18.95, 24.76, 25.14, 30.43, 32.14, 35.94, 51.87, 55.18, 55.84, 65.39, 76.39, 127.19, 128.35, 129.40, 132.97, 166.03 and 171.85; *m*/*z* (CI) 479 (M^+ + 18, 10%), 463 (M^+ + 2, 20), 462 (M^+ + 1, 78), 181(50) and 137 (100); δ_F-70.3; followed by the more polar, minor (2*R*)-epimer **146** as a colourless oil, $[\alpha]_D$ +1.9 (*c* 0.34 in DCM) (Found: M^+ + H, 462.2473. $C_{23}H_{35}O_5NF_3$ requires *M*, 462.2467); ν_{max}/cm^{-1} 732, 1102, 1164, 1464,1512, 1695, 1740, 2931 and 3379; δ_H (300 MHz, $CDCl_3$) 0.97 (3 H, t, *J* 7.5, CH_3CH_2), 1.15 (3 H, d, *J* 6.5, 8-H_3), 1.34–1.47 (6 H, m, 4-H_2, 5-H_2 and CH_3CH_2), 1.65 (2 H, m, 6-H_2), 1.79 and 1.99 (each 1 H, m, 3-H), 3.30 (1 H, m, 7-H), 3.34 (3 H, s, 7-OCH_3), 3.40 (3 H, d, *J* 1, CH_3O), 4.19 (2 H, m, CH_2CH_2O), 4.66 (1 H, dt, *J* 8 and 7.5, 2-H), 7.42–7.46 (4 H, m, ArH and NH) and 7.56–7.59 (2 H, m, ArH); *m*/*z* (CI) 479 (M^+ + 18, 8%), 463 (M^+ + 2, 14), 462 (M^+ + 1, 56), 181 (52), 121 (52) and 58 (100); δ_F −70.7.

Butyl (2*S*,7*S*,4*E*)- and (2*R*,7*S*,4*E*)-2-benzylamino-7-methoxyoct-4-enoate 148 and 149

The general procedure using the (*S*)-methoxyhexenylstannane (***S*)-123** (107 mg, 0.265 mmol) in DCM (4 mL), the benzylimine **147** (116 mg, 0.260 mmol) in DCM (1.5 mL) and tin(IV) bromide in DCM (1 M, 265 μL, 0.265 mmol) after 22 h at −45 °C and chromatography using petrol–ether–triethylamine (70 : 29 : 1) as eluent gave the *title compounds* **148** and **149** (51 mg, 57%) as a colourless oil, $[\alpha]_D$ −16.7 (*c* 1.09 in DCM) (Found: M^+ + H, 334.2385. $C_{20}H_{32}O_3N$ requires *M*, 334.2382); ν_{max}/cm^{-1} 737, 971, 1095, 1181, 1455, 1731, 2963 and 3330; δ_H (300 MHz, $CDCl_3$) 0.98 (3 H, t, *J* 7.5, CH_3CH_2), 1.89 (3 H, d, *J* 6.5, 8-H_3), 1.43 (2 H, m, CH_3CH_2), 1.67 (2 H, m, CH_2CH_2O), 1.89 (1 H, br s, NH), 2.15 and 2.29 (each 1 H, dt, *J* 14 and 7, 6-H), 2.43 (2 H, t, *J* 6.5, 3-H_2), 3.27–3.40 (2 H, m, 2-H and 7-H), 3.34 (3 H, s, 7-OCH_3), 3.71 and 3.88 (each 1 H, d, *J* 13, PhHC*H*), 4.15 (2 H, t, *J* 7.5, CH_2CH_2O), 5.45 (1 H, dt, *J* 15 and 7.5, 5-H), 5.55 (1 H, dt, *J* 15 and 7.5, 4-H) and 7.27–7.35 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 13.63, 18.75, 19.09, 30.66, 36.58, 39.08, 51.90, 55.91, 60.50, 64.38, 76.44, 126.95, 127.31, 128.17, 128.27, 129.88, 139.73 and 174.66; *m*/*z* (CI) 334 (M^+ + 1, 100%).

The general procedure using a mixture of the 2-(benzylamino)-octenoates **148** and **149** (40 mg, 0.128 mmol), 10% Pd/C (73 mg, 69 μmol) and ammonium formate (44 mg, 0.690 mmol) after 1 h at room temperature gave a mixture of the 2-amino-octanoates **141** and **144** (28 mg, 96%) as a colourless oil, $[\alpha]_D$ +3.5 (*c* 1.3 in DCM).

The general procedure using mixture of the amino-esters **141** and **144** (36 mg, 0.146 mmol), (*S*)-Mosher's acid chloride

(30 μL, 0.160 mmol), triethylamine (106 μL, 0.73 mmol) and DMAP (6 mg) gave the (*R*)-Mosher's amides **142** and **145** (52 mg, 77%), **142** : **145** = 86 : 14, samples of which were isolated by HPLC for characterization and comparison with a sample prepared earlier. Similarly, the amino-esters **141** and **144** (13 mg, 0.538 mmol), (*R*)-Mosher's acid chloride (12 μl, 59 μmol), triethylamine (40 μl, 0.276 mmol) and DMAP (6 mg) furnished the (*S*)-Mosher's amides **143** and **146** (18 mg, 71%), **143** : **146** = 86 : 14, samples of which were isolated by HPLC for characterization and comparison with other samples.

Butyl (2*S*,7*S*,4*E*)- and (2*R*,7*S*,4*E*)-7-hydroxy-2-[(*S*)-(1-phenylethyl)amino]oct-4-enoate 150 and 151

The general procedure using the (*S*)-hydroxyhexenylstannane (***S*)-122** (73 mg, 0.186 mmol) in DCM (2 mL), tin(IV) bromide in DCM (1 M, 186 μL, 0.186 mmol) and the (*S*)-imine (***S*)-11** (42 mg, 0.181 mmol) in DCM (1 mL) after 24 h at −45 °C for 24 h and chromatography using petrol–ether–triethylamine (70 : 29 : 1) as eluent gave the *title compounds* **150** and **151** (42 mg, 69%) as a colourless oil, **151** : **150** = 87 : 13 (^{1}H NMR). Samples were separated by preparative scale HPLC using hexane–ethyl acetate (1 : 1) as the eluent to give the less polar, minor (2*S*)-epimer **150** as a colourless oil, $[\alpha]_D$ −48.8 (*c* 0.83 in DCM) (Found: M^+ + H, 334.2386. $C_{20}H_{32}NO_3$ requires *M*, 334.2382); ν_{max}/cm^{-1} 702, 763, 970, 1025, 1183, 1274, 1453, 1731, 2963 and 3455; δ_H (500 MHz, $CDCl_3$) 0.99 (3 H, t, *J* 7.5, C*H*$_3$CH$_2$), 1.15 (3 H, d, *J* 6.5, 8-H$_3$), 1.31 (3 H, d, *J* 6.5, NHCHC*H*$_3$), 1.36 (2 H, hex, *J* 7.5, CH$_3$C*H*$_2$), 1.59 (2 H, qn, *J* 7.5, C*H*$_2$CH$_2$O), 1.92 (2 H, br s, OH and NH), 2.05 and 2.17 (each 1 H, dt, *J* 14 and 7, 6-H), 2.28 (2 H, t, *J* 6.5, 3-H$_2$), 3.05 (1 H, t, *J* 6.5, 2-H), 3.69 (1 H, q, *J* 6.5, NHC*H*CH$_3$), 3.76 (1 H, m, 7-H), 4.10 (2 H, m, CH$_2$O), 5.41 (1 H, dt, *J* 15.5 and 7.5, 5-H), 5.43 (1 H, dt, *J* 15 and 7.5, 4-H), 7.22 (1 H, m, ArH) and 7.26–7.30 (4 H, m, ArH); *m*/*z* (CI) 334 (M^+ + 1, 100%); followed by the more polar, major (2*R*)-epimer **151** as a colourless oil, $[\alpha]_D$ −14.41 (*c* 2.6 in DCM) (Found: M^+ + H, 334.2377. $C_{20}H_{32}O_3N$ requires *M*, 334.2382); δ_H (500 MHz, $CDCl_3$) 0.89 (3 H, t, *J* 7.5, C*H*$_3$CH$_2$), 1.16 (3 H, d, *J* 6.5, 8-H$_3$), 1.31 (2 H, hex, *J* 7.5, CH$_3$C*H*$_2$), 1.32 (3 H, d, *J* 6.5, NHCHC*H*$_3$), 1.52 (2 H, qn, *J* 7.5, C*H*$_2$CH$_2$O), 2.03 (1 H, dt, *J* 13 and 6.5, 6-H), 2.15 (2 H, br s, OH and NH), 2.18 (1 H, dt, *J* 13 and 6.5, 6-H), 2.29 and 2.39 (each 1 H, dt, *J* 13 and 6.5, 3-H), 3.35 (1 H, t, *J* 6.5, 2-H), 3.72 (1 H, m, 7-H), 3.74 (1 H, q, *J* 6.5, NHC*H*CH$_3$), 3.96 (2 H, t, *J* 7.5, CH$_2$O), 5.42 (1 H, dt, *J* 15 and 7.5, 5-H), 5.46 (1 H, dt, *J* 15.5 and 7.5, 4-H), 7.21 (1 H, dd, *J* 8.5 and 4.5, ArH), 7.28 (4 H, d, *J* 4.5, ArH); δ_C (125 MHz, $CDCl_3$) 13.65, 19.06, 22.52, 22.75, 30.55, 36.24, 42.48, 56.17, 58.96, 64.53, 66.60, 126.78, 127.15, 128.39, 128.99, 130.10, 144.79 and 174.62; *m*/*z* (CI) 334 (M^+ + 1, 100%).

Butyl (2*S*,7*S*,4*E*)- and (2*R*,7*S*,4*E*)-7-hydroxy-2-[(*R*)-(1-phenylethyl)amino]oct-4-enoate 152 and 153

The general procedure using the (*S*)-hydroxyhexenylstannane (***S*)-122** (67 mg, 0.171 mmol) in DCM (2 mL), tin(IV) bromide in DCM (1 M, 171 μL, 0.171 mmol) and the (*R*)-imine (***R*)-11** (39 mg, 0.166 mmol) in DCM (1 mL) after 24 h at −45 °C and chromatography using petrol–ether–triethylamine (70 : 29 : 1) as eluent gave the *title compounds* **152** and **153** (31 mg, 55%) as a colourless oil, **152** : **153** = 74 : 26 (^{1}H NMR). Samples were isolated by preparative HPLC eluting with hexane–ethyl acetate (1 : 1) to give the less polar, minor (2*R*)-epimer **153** as a colourless oil, $[\alpha]_D$ +36 (*c* 0.42 in DCM) (Found: M^+ + H, 334.2393. $C_{20}H_{32}O_3N$ requires *M*, 334.2382); ν_{max}/cm^{-1} 701, 1181, 1273, 1453, 1731, 2963 and 3423; δ_H (500 MHz, $CDCl_3$) 0.91 (3 H, t, *J* 7.5, C*H*$_3$CH$_2$), 1.17 (3 H, d, *J* 6.5, 8-H$_3$), 1.30 (3 H, d, *J* 6.5, NHCHC*H*$_3$), 1.34 (2 H, hex, *J* 7.5, CH$_3$C*H*$_2$), 1.58 (2 H, qn, *J* 7.5, C*H*$_2$CH$_2$O), 1.80 (2 H, br s, OH and NH), 2.03 and 2.18 (each 1 H, dt, *J* 13 and 6.5, 6-H), 2.24 and 2.31 (each 1 H, dt, *J* 13 and 6.5, 3-H), 3.06 (1 H, t, *J* 6.5, 2-H), 3.68 (2 H, q, *J* 6.5, HNC*H*CH$_3$), 3.73 (1 H, m, 7-H), 4.10 (2 H, m, CH$_2$O), 5.36–5.46 (2 H, m, 4-H and 5-H) and 7.19–7.30 (5 H, m, ArH); *m*/*z* (CI) 334 (M^+ + 1, 100%); followed by the more polar, major (2*S*)-epimer **152** as a colourless oil, $[\alpha]_D$ +27.5 (*c* 2.25 in DCM) (Found: M^+ + H, 334.2384. $C_{20}H_{32}O_3N$ requires *M*, 334.2382); ν_{max}/cm^{-1} 701,762, 971, 1125, 1183, 1453, 1731, 2963 and 3423; δ_H (500 MHz, $CDCl_3$) 0.89 (3 H, t, *J* 7.5, C*H*$_3$CH$_2$), 1.15 (3 H, d, *J* 6, 8-H$_3$), 1.31 (2 H, hex, *J* 7.5, CH$_3$C*H*$_2$), 1.33 (3 H, d, *J* 6.5, NHCHC*H*$_3$), 1.53 (2 H, qn, *J* 7.5, C*H*$_2$CH$_2$O), 2.05 (1 H, dt, *J* 14 and 7, 6-H), 2.15 (2 H, br s, OH and NH), 2.17 (1 H, dt, *J* 13.5 and 6.5, 6-H), 2.36 (2 H, t, *J* 6.5, 3-H$_2$), 3.32 (1 H, t, *J* 6.5, 2-H), 3.71–3.77 (2 H, m, 7-H and HNC*H*CH$_3$), 3.96 (2 H, t, *J* 7.5, C*H*$_2$O), 5.41–5.50 (2 H, m, 4-H and 5-H) and 7.21–7.31 (5 H, m, ArH); *m*/*z* (CI) 334 (M^+ + 1, 100%).

Methyl (2*S*,7*S*,4*E*)- and (2*R*,7*S*,4*E*)-7-hydroxy-2-[(2-nitrophenylsufanyl)amino]oct-4-enoate 154 and 158

The general procedure using the (*S*)-hydroxyhexenylstannane (***S*)-122** (66 mg, 0.169 mmol) in DCM (2 mL), tin(IV) bromide in DCM (1 M, 169 μL, 0.169 mmol) and the nitrophenylsulfanylimine **29** (39 mg, 0.164 mmol) in DCM (1 mL) after 24 h at −45 °C and chromatography using DCM–ether–triethylamine (90 : 9.5 : 0.5) as eluent gave the *title compounds* **154** and **158** (39 mg, 60%) as a yellow oil, $[\alpha]_D$ +3.3 (*c* 3.92 in DCM) (Found: M^+ + H, 341.1166. $C_{15}H_{21}O_5N_2S$ requires *M*, 341.1171); ν_{max}/cm^{-1} 736, 852, 973, 1098, 1208, 1337, 1447, 1511, 1566, 1592, 1738, 2964 and 3341; δ_H (500 MHz, $CDCl_3$) 1.17 (3 H, d, *J* 6.5, 8-H$_3$), 2.13 and 2.21 (each 1 H, dt, *J* 14 and 7, 6-H), 2.51 and 2.57 (each 1 H, dt, *J* 13 and 6.5, 3-H), 3.33 (1 H, d, *J* 8.5, NH), 3.56 (1 H, dt, *J* 8.5 and 6.5, 2-H), 3.74 (3 H, s, CH$_3$O), 3.79 (1 H, hex, *J* 6.5, 7-H), 5.48 (1 H, dt, *J* 15.5 and 7.5, 5-H), 5.58 (1 H, dt, *J* 15.5 and 7.5, 4-H), 7.22 and 7.60 (each 1 H, t, *J* 7.5, ArH), 8.03 (1 H, dd, *J* 7.5 and 0.5, ArH) and 8.22 (1 H, d, *J* 7.5, ArH); δ_C (125 MHz, $CDCl_3$) 22.81, 36.66, 42.31, 52.35, 63.51, 67.00, 124.49, 124.74, 125.71, 127.36, 131.33, 133.80, 142.47, 144.86 and 173.63; *m*/*z* (CI) 341 (M^+ + 1, 34%), 188 (100), 186 (22) and 126 (50).

Methyl (2*S*,7*S*,4*E*)- and (2*R*,7*S*,4*E*)-2-amino-7-hydroxyoct-4-enoate 155 and 159

Hydrogen chloride in methanol (1 M, 15 mL) was added to the mixture of nitrophenylsulfanylamines **154** and **158** (104 mg, 0.263 mmol) at room temperature and the suspension was stirred

for 2 h before concentration under reduced pressure. The solid residue was suspended in DCM (10 mL) and extracted with aqueous hydrogen chloride (1 M, 3 × 5 mL). The aqueous phase was basified by addition of solid sodium hydrogen carbonate until the solution had a pH ~10. The solution was then extracted with ethyl acetate (7 × 8 mL) and the organic extracts dried ($MgSO_4$), and concentrated under reduced pressure to leave the *title compounds* **155** and **159** (48 mg, 97%) as a pale yellow oil, $[\alpha]_D$ +6.9 (*c* 1.30 in DCM) (Found: M^+ + H, 188.1295. $C_9H_{18}O_3N$ requires *M*, 188.1287); ν_{max}/cm^{-1} 736, 974, 1208, 1438, 1738, 2963 and 3306; δ_H (300 MHz, $CDCl_3$) 1.22 (3 H, d, *J* 6.5, 8-H_3), 2.02 (3 H, br s, OH and NH_2), 2.18 (2 H, m, 6-H_2), 2.45 (2 H, m, 3-H_2), 3.69 (1 H, m, 2-H), 3.76 (3 H, s, CH_3O), 3.84 (1 H, m, 7-H) and 5.44–5.64 (2 H, m, 4-H and 5-H); δ_C (75 MHz, $CDCl_3$) 22.65, 42.23, 51.96, 66.90, 128.36 and 130.53; *m*/*z* (CI) 189 (M^+ + 2, 12%) and 188 (M^+ + 1, 100).

Methyl (2*S*,7*S*,4*E*)- and (2*R*,7*S*,4*E*)-7-hydroxy-2-[(*R*)-2-methoxy-2-phenyl-3,3,3-trifluoropropanoyl]amino-oct-4-enoate 156 and 160

(*S*)-Mosher's acid chloride (15 μL, 71.4 μmol) in chloroform (300 μL) was added dropwise to a vigorously stirred mixture of the amino alcohols **155** and **159** (11 mg, 56.1 μmol) and solid sodium hydrogen carbonate (30 mg, 0.361 mmol) in chloroform (2 mL) containing distilled water (0.5 mL) at room temperature. The mixture was stirred vigorously at room temperature overnight then diluted with saturated aqueous sodium hydrogen carbonate and extracted with DCM (4 × 5 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using petrol–ether (50 : 50) as eluent gave the *title compounds* **156** and **160** (16 mg, 69%) as a pale yellow oil, **156** : **160** = 86 : 14 (^1H and ^{19}F NMR), $[\alpha]_D$ −2.83 (*c* 2.12 in DCM) (Found: M^+ + H, 404.1696. $C_{19}H_{25}O_5NF_3$ requires *M*, 404.1685); ν_{max}/cm^{-1} 977, 1106, 1167, 1270, 1440, 1515, 1692, 1745, 2960 and 3412; δ_H (300 MHz, $CDCl_3$) 1.15 (0.42 H, d, *J* 6.5, 8-H_3), 1.22 (2.58 H, d, *J* 6.5, 8-H_3), 1.74 (1 H, br s, OH), 2.10 (2 H, m, 6-H_2), 2.62 (2 H, m, 3-H_2), 3.39 (2.58 H, d, *J* 1.5, CH_3O), 3.55 (0.42 H, d, *J* 1.5, CH_3O), 3.80 (2.58 H, s, CH_3O), 3.79 (0.42 H, s, CH_3O), 3.84 (1 H, m, 7-H), 4.73 (1 H, m, 2-H), 5.25–5.53 (0.28 H, m, 4-H and 5-H), 5.45 (0.86 H, dt, *J* 15 and 7.5, 5-H), 5.62 (0.86 H, dt, *J* 15 and 7.5, 4-H), 7.20 (0.14 H, d, *J* 8, NH), 7.49 (0.86 H, d, *J* 8, NH), 7.44–7.50 (3 H, m, ArH) and 7.55–7.58 (2 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 22.68, 35.15, 42.27, 51.83, 52.45, 54.82, 66.92, 126.63, 127.97, 128.39, 128.52, 129.49, 131.73, 165.86 and 171.54; *m*/*z* (CI) 421 (M^+ + 18, 34%), 405 (M^+ + 2, 20), 404 (M^+ + 1, 100) and 213 (60); δ_F −70.4 (minor), −70.7 (major).

Methyl (2*S*,7*S*,4*E*)- and (2*R*,7*S*,4*E*)-7-hydroxy-2-[(*S*)-2-methoxy-2-phenyl-3,3,3-trifluoropropanoyl]amino-oct-4-enoate 157 and 161

The above procedure using (*R*)-Mosher's acid chloride (20 μL, 0.108 μmol), the amino alcohols **155** and **159** (17 mg, 90.3 μmol) and solid sodium hydrogen carbonate (50 mg, 0.542 mmol) in chloroform (2 mL) containing distilled water (0.5 mL) after stirring for 15 h and chromatography eluting with petrol–ether (50 : 50) gave the *title compounds* **157** and **161** (23 mg, 64%) as a pale yellow oil, **157** : **161** = 86 : 14 (^1H and ^{19}F NMR), $[\alpha]_D$ −2.83 (*c* 2.12 in DCM) (Found: M^+ + H, 404.1689. $C_{19}H_{25}O_5NF_3$ requires *M*, 404.1685); ν_{max}/cm^{-1} 721, 1106, 1166, 1270, 1440, 1511, 1690, 1744, 2958 and 3415; δ_H (300 MHz, $CDCl_3$) 1.05 (2.58 H, d, *J* 6.5, 8-H_3), 1.12 (0.42 H, d, *J* 6.5, 8-H_3), 1.48 (1 H, br s, OH), 2.04 (2 H, m, 6-H_2), 2.44 (2 H, t, *J* 6.5, 3-H_2), 3.29 (0.42 H, s, CH_3O), 3.47 (2.58 H, s, CH_3O), 3.56 (1 H, m, 7-H), 3.69 (0.42 H, s, CH_3O), 3.70 (2.58 H, s, CH_3O), 4.65 (1 H, m, 2-H), 5.14–5.58 (2 H, m, 4-H and 5-H), 7.08 (0.86 H, d, *J* 8, NH), 7.32–7.36 (3.14 H, m, ArH and NH) and 7.46–7.52 (2 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 22.75, 35.08, 42.10, 51.57, 52.51, 55.22, 66.78, 126.45, 127.25, 128.38, 129.42, 131.66, 166.10 and 171.46; *m*/*z* (CI) 421 (M^+ + 18, 18%), 405 (M^+ + 2, 20) and 404 (M^+ + 1, 100); δ_F −70.4 (major), −70.7 (minor).

Methyl glyoxylate *O*-benzyloxime 165

A suspension of freshly prepared methyl glyoxylate (1.75 g, 19.9 mmol) and *O*-benzyl hydroxylamine hydrochloride (3.17 g, 19.9 mmol) was heated under reflux in toluene (100 mL) with azeotropic removal of water for 12 h. After cooling to ambient temperature and concentration under reduced pressure, the residue was applied directly to a short column of silica gel. Elution with hexane–ethyl acetate (95 : 5) gave the *title compound* **165** (3.5 g, 91%) as a colourless liquid (Found: M^+ + H, 194.0813. $C_{10}H_{12}NO_3$ requires *M*, 194.0817); ν_{max}/cm^{-1} 699, 732, 923, 1005, 1046, 1207, 1274, 1330, 1368, 1441, 1599, 1727, 2952 and 3032; δ_H (300 MHz, $CDCl_3$) 3.89 (3 H, s, CH_3), 5.34 (2 H, s, $PhCH_2O$), 7.40–7.42 (5 H, m, ArH) and 7.60 (1 H, s, HC = N); δ_C (75 MHz, $CDCl_3$) 52.56, 78.17, 128.55, 128.60, 128.62, 135.92, 140.92 and 162.41; *m*/*z* (CI) 211 (M^+ + 18, 100%) and 194 (M^+ + 1, 30).

Methyl glyoxylate oxime 166

A suspension of freshly prepared methyl glyoxylate (4.40 g, 50.0 mmol) and hydroxylamine hydrochloride (3.47 g, 50.0 mmol) was heated under reflux in toluene (100 mL) with azeotropic removal of water for 12 h. After cooling to ambient temperature, concentration under reduced pressure gave an oil that crystallised on standing. This solid was stirred with hexane–ether (10 : 1) for 1 h, then filtered off and dried under a high vacuum (0.1 mm Hg) to afford the *title compound* **166** (4.4 g 85%) as a pale yellow powder, m.p. 53–55 °C (Found: C, 34.8; H, 6.0; N, 13.1. $C_{10}H_{13}NO$ requires C, 34.6; H, 5.8; N, 13.5); ν_{max}/cm^{-1} 757, 1031, 1219, 1264, 1318, 1451, 1625, 1727, 2959 and 3330; δ_H (200 MHz, $CDCl_3$) 3.85 (3 H, s, CH_3O) and 7.57 (1 H, s, HC = N); δ_C (50 MHz, $CDCl_3$) 53.18, 142.08 and 163.37; *m*/*z* (CI) 121 (M^+ + 18, 100%) and 105 (M^+ + 1, 35).

Methyl glyoxylate *N*-tosylhydrazone 167

A solution of freshly prepared methyl glyoxylate (3.50 g, 39.7 mmol) and toluene 4-sulfonylhydrazine (7.40 g, 39.7 mmol) was heated under reflux in toluene (100 mL) for

12 h with azeotropic removal of water. After cooling to ambient temperature, concentration under reduced pressure gave a white solid that was stirred with ether for 1 h, then filtered and dried under high vacuum (0.1 mm Hg) to afford the *title compound* **167** (10.0 g, 98%) as a white powder m.p. 114–115 °C (Found: C, 47.1; H, 4.85; N, 10.9; S, 12.2. $C_{10}H_{12}N_2O_4S$ requires C, 46.9; H, 4.7; N, 10.9; S, 12.5); ν_{max}/cm^{-1} 664, 741, 818, 870, 960, 984, 1059, 1172, 1230, 1364, 1440, 1594, 1711, 2961 and 3175; δ_H (300 MHz, $CDCl_3$) 2.46 (3 H, s, $PhCH_3$), 3.83 (3 H, s, CH_3O), 6.86 (1 H, s, HC═N), 7.36 (2 H, d, *J* 8.2, ArH), 7.86 (2 H, d, *J* 8.3, ArH) and 12.09 (1 H, br s, NH); δ_C (75 MHz, $CDCl_3$) 21.66, 52.38, 127.54, 127.90, 129.86, 135.24, 144.74 and 162.06; *m*/*z* (CI) 274 (M^+ + 18, 100%) and 257 (M^+ + 1, 5).

Methyl (*RS*)-2-(benzyloxyamino)pent-4-enoate 168

The general procedure using tin(IV) chloride (391 mg, 1.50 mmol) in DCM (5 mL), prop-2-enyl(tributyl)stannane **3** (521 mg, 1.57 mmol) in DCM (5 mL) and the oxime-ether **165** (304 mg, 1.57 mmol) after 4 h at −78 °C and chromatography using petrol–ethyl acetate–triethylamine (95 : 4.5 : 0.5) as eluent gave the *title compound* **168** (288 mg, 82%) as a colourless liquid (Found: M^+ + H, 236.1282. $C_{13}H_{18}NO_3$ requires *M*, 236.1287); ν_{max}/cm^{-1} 698, 741, 919, 995, 1203, 1363, 1438, 1741, 2951 and 3263; δ_H (300 MHz, $CDCl_3$) 2.36–2.43 (2 H, m, 3-H_2), 3.78 (1 H, m, 2-H), 3.78 (3 H, s, CH_3O), 4.75 (2 H, s, $PhCH_2O$), 5.10–5.17 (2 H, m, 5-H_2), 5.76 (1 H, m, 4-H), 5.99 (1 H, d, *J* 9, NH) and 7.30–7.42 (5 H, m, ArH); δ_C (75 MHz, $CDCl_3$) 33.88, 51.99, 63.29, 76.28, 118.16, 127.87, 128.35, 128.50, 133.08, 137.67 and 173.64; *m*/*z* (CI) 236 (M^+ + 1, 100%).

Methyl (*RS*)-2-(hydroxyamino)pent-4-enoate 169

The general procedure using tin(IV) chloride (391 mg, 1.50 mmol) in DCM (5 mL), prop-2-enylstannane **3** (521 mg, 1.57 mmol) in DCM (5 mL) and the oxime **166** (163 mg, 1.57 mmol) in DCM (5 mL) after 4 h at −78 °C and chromatography using hexane–ethyl acetate–triethylamine (60 : 39.5 : 0.5) as eluent gave the *title compound* **169** (174 mg, 80%) as a colourless oil which crystallised on standing. Recrystallisation from ether–hexane gave the hydroxylamine as white needles, m.p. 49–50 °C (Found: C, 50.0; H, 7.5; N, 9.5. $C_6H_{11}NO_3$ requires C, 49.65; H, 7.65; N, 9.7); ν_{max}/cm^{-1} 923, 996, 1204, 1225, 1438, 1642, 1742, 2954, 3269 and 3426; δ_H (300 MHz, $CDCl_3$) 2.31–2.50 (2 H, m, 3-H_2), 3.75 (1 H, dd, *J* 7.8 and 6.8, 2-H), 3.79 (3 H, s, CH_3O), 5.10–5.20 (2 H, m, 5-H_2), 5.61 (1 H, br s, OH), 5.76 (1 H, m, 4-H) and 6.75 (1 H, br s, NH); δ_C (75 MHz, $CDCl_3$) 33.71, 52.10, 64.43, 118.66, 132.78 and 173.41; *m*/*z* (CI) 163 (M^+ + 18, 10%), 146 (M^+ + 1, 55), 130 (100) and 128 (40).

Methyl (*RS*)-2-(toluene-4-sulfonylhydrazino)pent-4-enoate 170

The general procedure using tin(IV) chloride (521 mg, 2.0 mmol) in DCM (8 mL), prop-2-enyl(tributyl)stannane (695 mg, 2.1 mmol) in DCM (8 mL) and the hydrazone **167** (538 mg, 2.1 mmol) in DCM (8 mL) after 50 h at −78 °C and chromatography using hexane–ether (1 : 1) as eluent gave the *title compound* **170** (365 mg, 61%) as a colourless oil (Found: M^+ + H, 299.1067. $C_{13}H_{19}N_2O_4S$ requires *M*, 299.1066); ν_{max}/cm^{-1} 812, 922, 987, 1092, 1162, 1211, 1330, 1438, 1598, 1733, 2953, 3250 and 3306; δ_H (300 MHz, $CDCl_3$) 2.25–2.45 (2 H, m, 3-H_2), 2.42 (3 H, s, $PhCH_3$), 3.60 (1 H, dd, *J* 6.9 and 5.2, 2-H), 3.71 (3 H, s, CH_3O), 3.90 (1 H, dd, *J* 9.8 and 5.2, CHN*H*), 5.01–5.07 (2 H, m, 5-H_2), 5.60 (1 H, m, 4-H), 6.29 (1 H, d, *J* 5.2, CHNHN*H*), 7.29 (2 H, d, *J* 8.3, ArH) and 7.77 (2 H, d, *J* 8.1, ArH); δ_C (75 MHz, $CDCl_3$) 21.68, 34.78, 52.28, 62.93, 118.42, 128.12, 129.41, 132.38, 134.86, 143.88 and 173.57; *m*/*z* (CI) 299 (M^+ + 1, 35%) and 143 (100).

Methyl (2*R*,6*S*,*E*)- and (2*S*,6*S*,*E*)-6-benzyloxy-2-(benzyloxyamino)hept-4-enoates 171 and 173

The general procedure using tin(IV) chloride (296 mg, 1.13 mmol) in DCM (5 mL), the 4-benzyloxypentenylstannane **1** (555 mg, 1.19 mmol) in DCM (5 mL) and the oxime-ether **165** (230 mg, 1.19 mmol) in DCM (5 mL) after 50 h at −45 °C and chromatography using hexane–ethyl acetate–triethylamine (95 : 4.5 : 0.5) as eluent gave the *title compounds* **171** and **173** (281 mg, 67%) as a colourless oil, **171** : **173** = 90 : 10 (^{1}H NMR) (Found: M^+ + H, 370.2025. $C_{22}H_{28}NO_4$ requires *M*, 370.2018); ν_{max}/cm^{-1} 698, 738, 973, 1072, 1208, 1366, 1451, 1742, 2862 and 3264; δ_H (300 MHz, $CDCl_3$) major isomer 1.30 (3 H, d, *J* 6.3, 7-H_3), 2.32–2.42 (2 H, m, 3-H_2), 3.74 (1 H, m, 2-H), 3.78 (3 H, s, CH_3O), 3.91 (1 H, qn, *J* 6.4, 6-H), 4.38 and 4.56 (each 1 H, d, *J* 12, PhHC*H*O), 4.75 (2 H, s, $PhCH_2$), 5.48–5.63 (2 H, m, 4-H and 5-H), 5.98 (1 H, d, *J* 9.4, NH) and 7.14–7.41 (10 H, m, ArH); δ_H (500 MHz, C_6D_6) major isomer 5.46 (1 H, dd, *J* 15.5 and 7.4, 5-H) and 5.51 (1 H, dt, *J* 15.5 and 6.4, 4-H); δ_H (300 MHz, $CDCl_3$) minor isomer 1.25 (d, *J* 6.3, 7-H_3), 3.77 (s, CH_3O), 4.33 and 4.50 (each d, *J* 11.8, PhHC*H*) and 4.74 (s, $PhCH_2O$); δ_C (75 MHz, $CDCl_3$) major isomer 21.63, 32.43, 52.05, 63.50, 69.80, 75.29, 76.28, 126.94, 127.46, 127.69, 127.90, 128.38, 128.48, 128.85, 135.74, 137.68, 138.80 and 173.59; minor isomer 21.56, 32.37, 68.15, 75.61, 125.99, 126.46, 126.90, 129.20, 130.47, 135.69, 139.20 and 140.66; *m*/*z* (CI) 370 (M^+ + H, 50%) and 262 (100).

Methyl (2*R*,6*S*,*E*)- and (2*S*,6*S*,*E*)-6-benzyloxy-2-(hydroxyamino)-hept-4-enoates 172 and 174

The general procedure using tin(IV) chloride (417 mg, 1.60 mmol) in DCM (5 mL), 4-benzyloxypentenylstannane **1** (782 mg, 1.68 mmol) in DCM (5 mL) and the oxime **166** (175 mg, 1.68 mmol) in DCM (5 mL) after 50 h at −78 °C and chromatography using hexane–ethyl acetate–triethylamine (60 : 39.5 : 0.5) as eluent gave the *title compounds* **172** and **174** (286 mg, 64%) as a pale yellow oil, **172** : **174** = 87 : 13 (^{1}H NMR) (Found: M^+ + H, 280.1538. $C_{15}H_{22}NO_4$ requires M, 280.1549); ν_{max}/cm^{-1} 699, 737, 1072, 1210, 1440, 1453, 1742, 2865, 2973, 3270 and 3410; δ_H (300 MHz, $CDCl_3$) major isomer 1.30 (3 H, d, *J* 6.3, 7-H_3), 2.39–2.54 (2 H, m, 3-H_2), 3.77 (1 H, m, 2-H), 3.79 (3 H, s, CH_3O), 3.89 (1 H, m, 6-H), 4.40 (1 H, d, *J* 11.9, PhHC*H*), 4.45 (1 H, br s, OH), 4.57 (1 H, d, *J* 11.9, PhHC*H*), 5.51–5.69 (2 H, m, 4-H and 5-H), 6.10 (1 H,

br s, NH) and 7.29–7.38 (5 H, m, ArH); minor isomer 1.29 (d, *J* 6.3, 7-H_3) and 4.37 and 4.53 (each d, *J* 11.9, PhHC*H*); *m*/*z* (CI) 280 (M^+ + 1, 6%), 264 (12) and 172 (100).

Methyl (2*R*,6*S*)- and (2*S*,6*S*)-6-benzyloxy-2-(benzyloxyamino)-heptanoate 175 and 176

The general procedure using the heptenoates **171** and **173** (445 mg, 0.541 μmol, **171** : **173** = 9 : 1), toluene 4-sulfonylhydrazine (1.01 g, 5.42 mmol) and anhydrous sodium acetate (444 mg, 5.41 mmol) after chromatography using hexane–ethyl acetate (9 : 1) as eluent gave the *title compounds* **175** and **176** (193 mg, 96%), **175** : **176** = 85 : 15 (^{1}H NMR) as a colourless oil (Found: M^+ + H, 372.2163. $C_{22}H_{30}NO_4$ requires *M*, 372.2163); ν_{max}/cm^{-1} 697, 736, 1065, 1205, 1452, 1495, 1740, 2864, 2948 and 3336; δ_H (300 MHz, $CDCl_3$) major isomer 1.21 (3 H, d, *J* 6.1, 7-H_3), 1.40–1.61 (6 H, m, 3-H_2, 4-H_2 and 5-H_2), 3.46–3.68 (2 H, m, 2-H and 6-H), 3.79 (3 H, s, CH_3O), 4.47 and 4.60 (each 1 H, d, *J* 11.9, PhHC*H*), 4.72 (2 H, s, $PhCH_2O$), 5.97 (1 H, d, *J* 10.0, NH) and 7.30–7.40 (10 H, m, ArH); minor isomer 1.18 (d, *J* 6.1, 7-H_3), 3.78 (s, CH_3O), 4.40 and 4.57 (each d, *J* 11.9, PhHC*H*) and 4.71 (s, $PhCH_2O$); δ_C (75 MHz, $CDCl_3$) major isomer 19.59, 22.11, 29.65, 36.33, 51.94, 63.75, 70.35, 74.46, 76.15, 127.45, 127.64, 127.81, 128.32, 128.35, 128.51, 137.85, 139.03 and 174.68; minor isomer 19.48, 38.32, 68.41, 74.66, 126.02, 126.47, 128.43, 128.81, 129.13, 130.41 and 136.92; *m*/*z* (CI) 372 (M^+ + 1, 100%), 266 (90) and 264 (60).

The general procedure for transfer hydrogenolysis using the heptanoates **175** and **176** (170 mg, 0.458 μmol, **175** : **176** = 85 : 15) gave an amino-alcohol that was acetylated using triethylamine (383 μL, 2.75 mmol), acetic anhydride (130 μL, 1.37 mmol) and DMAP (3 mg, 25 μmol) to give, after chromatography using chloroform–methanol (99 : 1) as eluent, the heptanoate **43** (105 mg, 88%) as a colourless oil containing *ca.* 10% of its epimer **73** (^{1}H NMR).

Crystal data for carbamate 14

$C_{22}H_{30}Cl_3NO_4$, MW 478.82, triclinic, space group $P\bar{1}$, *a* = 11.185(5), *b* = 11.22(1), *c* = 10.307(5) Å, α = 104.76(5), β = 91.60(4), γ = 100.21(5)°, *V* = 1227.2(14) Å^3, *Z* = 2, D_c = 1.296 g cm^{-3}, μ(CuKα) = 3.603 mm^{-1}, *F*(000) = 504, *T* = 295 K. Crystal dimensions were 0.55 × 0.33 × 0.28 mm. 3848 reflections measured, 3630 independent reflections (R_{int} = 0.15), R_1 = 0.073 for the 2627 reflections with $I > 2\sigma(I)$, w$R(F^2)$ = 0.233 (all data); CCDC 862199.‡

Crystal data for the 2-(alkylamino)lactone 25

$C_{20}H_{21}NO_4$, MW 339.38, orthorhombic, space group $P2_12_12_1$, *a* = 9.681(3), *b* = 28.33(1), *c* = 6.260(2), Å, *V* = 1716.9(11) Å^3, *Z* = 4, Dc = 1.313 g cm^{-3}, μ(CuKα) = 0.746 mm^{-1}, *F*(000) = 720, *T* = 295 K. Crystal dimensions were 0.45 × 0.25 × 0.01 mm. 1503 independent reflections, R_1 = 0.074 for the 1045 reflections with $I > 2\sigma(I)$, $R_w(F)$ = 0.192(all data); CCDC 862200.‡

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