Regiospecific ring-opening reactions of β-aziridinyl α,β-enoates with acids: application to the stereoselective synthesis of a couple of diastereoisomeric (*E*)-alkene dipeptide isosteres from a single β-aziridinyl α,β-enoate and to the convenient preparation of amino alcohols bearing α,β-unsaturated ester groups

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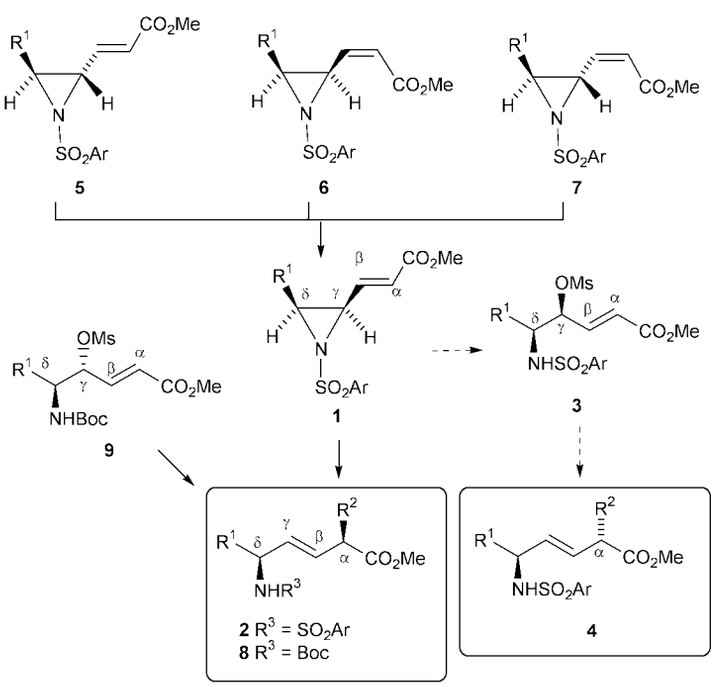
Regio- and stereo-selective ring-opening reactions of *N*-(2,4,6-trimethylphenylsulfonyl)-γ,δ-*cis*- or -*trans*-γ,δ-epimino (*E*)-α,β-enoates with acids such as methanesulfonic acid (MSA) or trifluoroacetic acid (TFA) have been found. These ring-opening reactions are useful for the stereoselective synthesis of a couple of diastereomeric (*E*)-alkene dipeptide isosteres from a single substrate of γ,δ-epimino (*E*)-α,β-enoate, and for the convenient preparation of δ-aminated γ-hydroxy α,β-enoates.

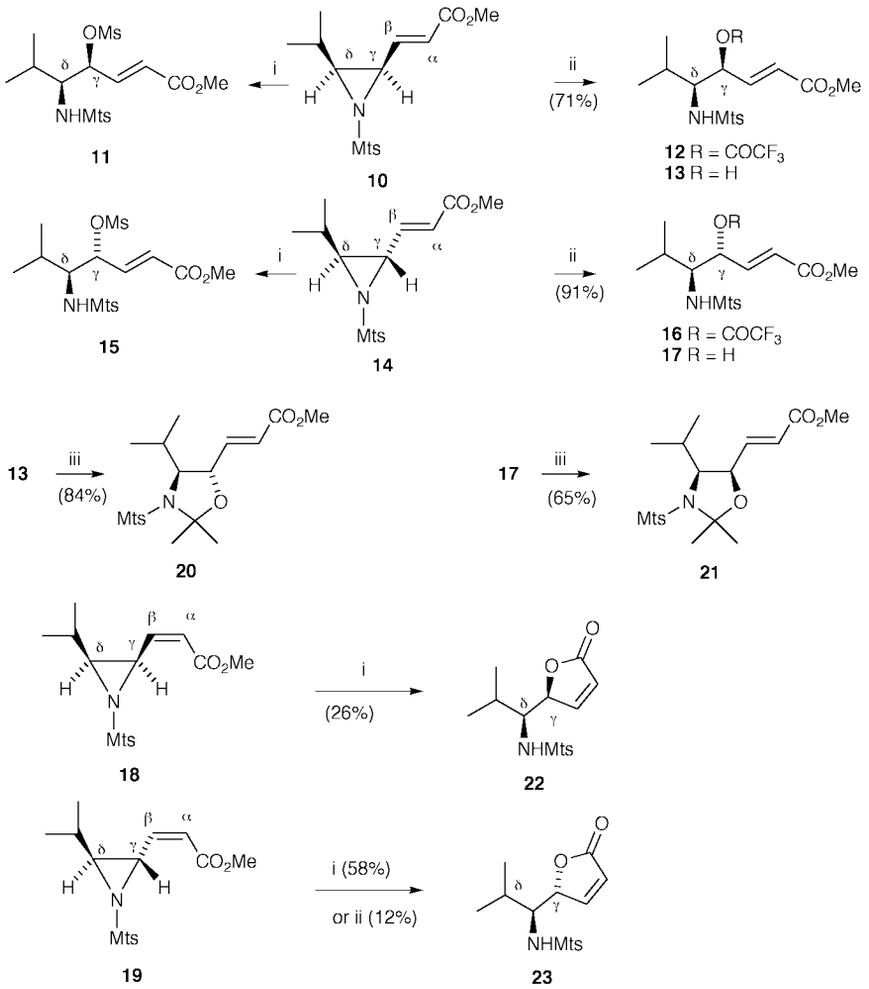
Introduction

The potential of (*E*)-alkene dipeptide isosteres as backbone replacements of amide bonds in peptides has been well documented among various dipeptide isosteres in the past few years.[1] We[2] and others[3] have recently reported that peptides containing (*E*)-alkene isosteres can exhibit potent biological activities. In order to facilitate structure–activity relationship studies on such peptide-lead candidates, development of new efficient methodology for the synthesis of (*E*)-alkene isosteres is needed. Since it has been reported that the stereochemistry at the α-position and the (*E*)-configuration are important for biological activity, the stereocontrolled synthesis of both isomers of types **2** and **4** from a single substrate of type **1** would be extremely valuable (Scheme 1). One advantage of such a strategy is that three other stereoisomeric enoates **5**, **6**, and **7** can be convergently transformed into the enoate **1** by exposure to a palladium(0)-catalyst (Scheme 1).[4] We and others reported previously the two synthetic methods for diastereomerically pure (*E*)-alkene isosteres **2** and **8** by employing organocopper-mediated *anti*-S_N2' reactions of β-aziridinyl α,β-enoate **1**[5] and δ-aminated γ-mesyloxy α,β-enoate **9**,[6] respectively.

As part of our investigations of peptide scaffold designs related to structure–activity relationship studies, we are particularly interested in ring-opening reactions of enoates of type **1** for the preparation of key intermediates **3** for the synthesis of dipeptide surrogates **4**. In this paper, we detail the regio- and stereo-specific ring-opening reactions of β-aziridinyl α,β-



Scheme 1 R^1, R^2 = alkyl; Ar = 4-methylphenyl or 2,4,6-trimethylphenyl, Ms = methanesulfonyl.



Scheme 2 *Reagents*: i, CH_3SO_3H; ii, CF_3CO_2H; iii, 2,2-dimethoxypropane, pyridinium toluene-*p*-sulfonate; Mts = 2,4,6-trimethylphenylsulfonyl.

enoates by methanesulfonic acid (MSA) and the stereoselective synthesis of (*E*)-alkene dipeptide isosteres by treatment of the ring-opened products with organocopper reagents.[7] In addition, we also report our finding of similar ring-opening reactions by trifluoroacetic acid (TFA) and the application of such reactions to a convenient synthesis of homochiral δ-aminated γ-hydroxy α,β-enoates, such as a versatile building block for sphingosine synthesis.

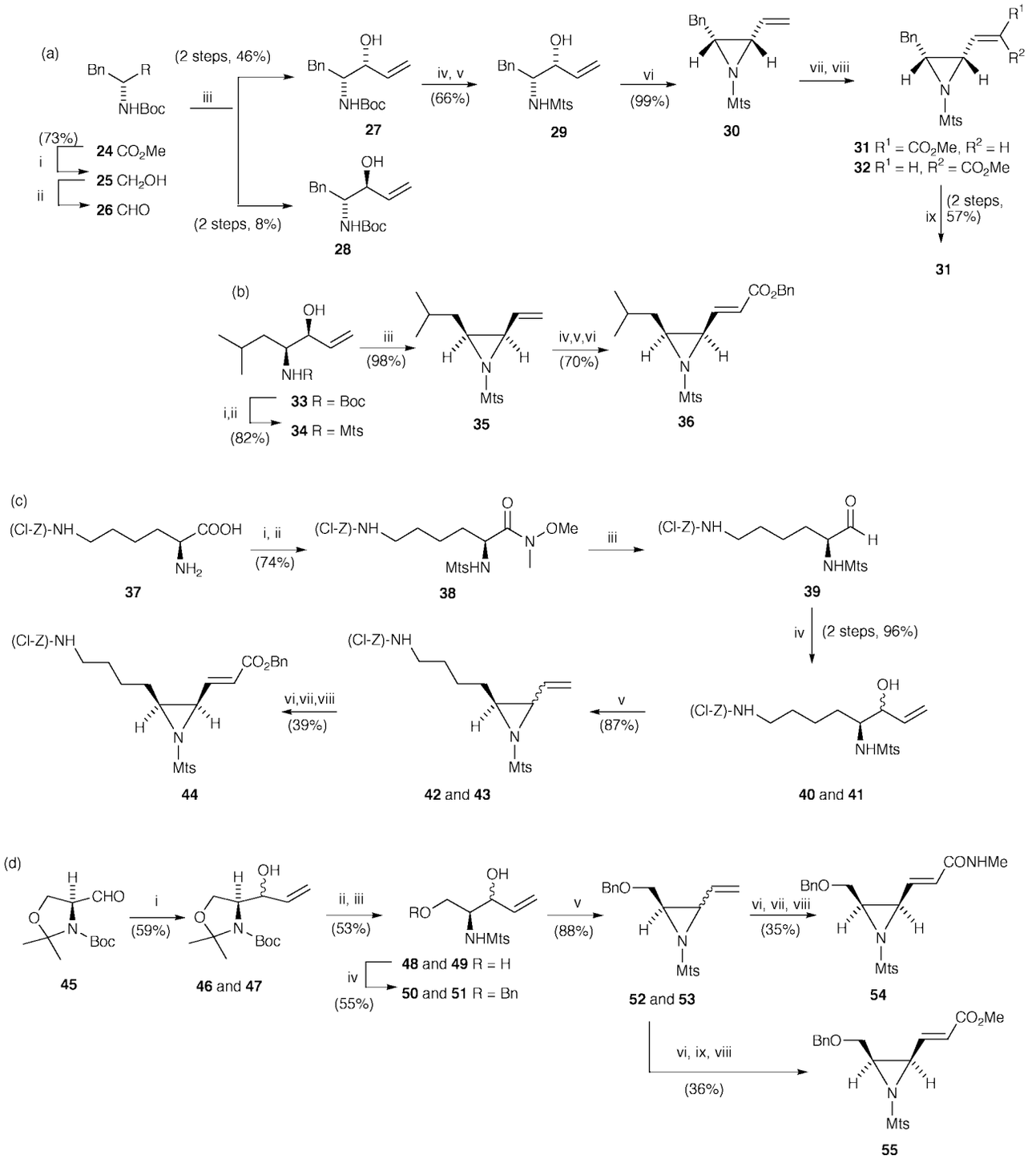
The focus of this paper deals with regiospecific ring-opening reactions of β-aziridinyl α,β-enoates and their applications.

Results and discussion

Ring-opening reactions of *N*-(2,4,6-trimethylphenylsulfonyl) (Mts)-γ,δ-epimino α,β-enoates with MSA or TFA

Although there exist ample precedents demonstrating that various nucleophiles,[8] containing acids such as acetic acid,[9] TFA[10] and toluene-*p*-sulfonic acid in aqueous acetone,[11] attack simple *N*-activated or inactivated aziridines[12] at either of two carbon atoms, yielding the corresponding ring-opened products, the practically useful reactions involving γ,δ-epimino α,β-enoates of type **1** with MSA or TFA have not been reported heretofore. We initially examined ring-opening reactions by MSA treatment of *N*-(2,4,6-trimethylphenylsulfonyl) (Mts)-protected (and activated) aziridines bearing α,β-unsaturated esters[4,5] (Scheme 2). Exposure of the *N*-Mts-γ,δ-*cis*-γ,δ-epimino (*E*)-α,β-enoate **10**, which was previously synthesized from L-valine,[4] to MSA (10 equiv.) in $CHCl_3$ at rt for 20 min afforded exclusively δ-aminated γ-mesyloxy α,β-enoate **11** in essentially quantitative yield, presumably *via* the regioselective S_N2 ring-opening reaction at the γ-carbon position. Furthermore, we investigated the feasibility of the ring-opening reactions by TFA treatment. The *cis*-(*E*)-enoate **10** was exposed to TFA at rt for 15 h to afford exclusively the δ-aminated γ-trifluoroacetoxy α,β-enoate **12**. Hydrolysis of **12** and silica gel flash chromatographic purification yielded the δ-aminated γ-hydroxy α,β-enoate **13** in 93% yield based on **10** (Scheme 2). It was found that the MSA-mediated ring-opening reaction proceeded much faster than the reaction involving TFA. In both cases, ring-opened products generated by nucleophilic attack at the α- or δ-carbon position could not be detected. Regiochemical assignments for the mesyl ester **11** and the trifluoroacetate **12** were readily made by ^{1}H-NMR (^{1}H–^{1}H COSY). The γ,δ-*syn* stereochemistry of the ring-opened product **13** was confirmed by transformation of **13** into the original substrate **10** using the Mitsunobu conditions.[13] Since the mesyl compound **11** was prone to regenerate the original substrate **10** during silica gel flash chromatographic purification, it could not be isolated in an analytically pure form.

Next, ring-opening of three other stereoisomeric enoates **14**, **18** and **19**, which were previously synthesized from L-valine,[4] was investigated. Regiospecific ring-opening was successfully carried out on the *trans*-(*E*)-isomer of the aziridine enoate **14** with MSA or TFA treatment in a similar manner, yielding **15** or **17**, respectively (the isolated yield of **17** based on **14**: 91%). In both cases, ring-opened products generated by nucleophilic attack at the α- or δ-carbon position could not be detected. Regiochemical assignments for the mesyl ester **15** and the trifluoroacetate **16** were readily made by ^{1}H–^{1}H COSY. The γ,δ-*anti* stereochemistry of the ring-opened product **17** was confirmed by transformation of **17** into the original substrate **14** using the Mitsunobu conditions.[13] Furthermore, stereo-



Scheme 3 (a) *Reagents*: i, DIBAL; ii, oxalyl dichloride, DMSO, DIPEA; iii, vinylMgCl; iv, TFA; v, Mts-Cl, Et_3N; vi, Ph_3P, DEAD; vii, O_3, dimethyl sulfide; viii, $Ph_3P{=}CHCO_2Me$; ix, $Pd(PPh_3)_4$; (b) *Reagents*: i, TFA; ii, Mts-Cl, Et_3N; iii, Ph_3P, DEAD; iv, O_3, dimethyl sulfide; v, $Ph_3P{=}CHCO_2Bn$; vi, $Pd(PPh_3)_4$; (c) *Reagents*: i, Mts-Cl, Et_3N; ii, HOBt, WSCD, *N*,*O*-dimethylhydroxylamine hydrochloride; iii, DIBAL; iv, vinylMgCl; v, Ph_3P, DEAD; vi, O_3, dimethyl sulfide; vii, $Ph_3P{=}CHCO_2Bn$; viii, $Pd(PPh_3)_4$; (d) *Reagents*: i, vinylMgCl; ii, TFA, H_2O; iii, Mts-Cl, DIPEA; iv, BnBr, NaH; v, Ph_3P, DEAD; vi, O_3, dimethyl sulfide; vii, $(EtO)_2P(O)CH_2CONHMe$, DIPEA; viii, $Pd(PPh_3)_4$; ix, $Ph_3P{=}CHCO_2Me$.

chemical assignments for diastereomers **13** and **17** were also easily established by conversion to the acetonide derivatives **20** and **21**, respectively. The NOE data by NMR analyses of **20** and **21** are in good agreement with their stereochemistry. On the other hand, attempted treatment of the *cis*-(*Z*)-enoate **18** and the *trans*-(*Z*)-enoate **19** with MSA or TFA failed to afford the desired ring-opened products and, instead, gave complex mixtures containing the γ-butenolactones, **22** and **23**, respectively. This clearly demonstrates that a slight difference in the structure of the substituents can significantly change the reaction route. Since the enoates **18** and **19** can be converted into the enoate **10** *via* Pd(0)-catalyzed reactions,[4] this ring-opening reaction incurs no significant problems in terms of its practical use for the preparation of (*E*)-alkene isosteres, although our methodology is not applicable to the synthesis of (*Z*)-alkene isosteres.

Synthesis of the other requisite *N*-Mts-γ,δ-*cis*-γ,δ-epimino (*E*)-α,β-enoates (enamides)

As shown in Scheme 3, the diastereomerically pure *N*-Mts-γ,δ-*cis*-γ,δ-epimino (*E*)-α,β-enoates (enamides) **31**, **36**, **44**, **54** and

55, which were required for the synthesis of (*E*)-alkene dipeptide isosteres (amino alcohols), were readily prepared according to the known methods.[4,5] Boc-D-Phe-OMe **24** was treated successively with diisobutylaluminium hydride (DIBAL), oxalyl dichloride– dimethyl sulfoxide (DMSO)–*N*,*N*-diisopropylethylamine (DIPEA) and vinylmagnesium chloride to give a separable 6:1 mixture of allyl alcohols **27** and **28**. Exposure of **27** to TFA followed by successive treatments with Mts-Cl in the presence of triethylamine (Et_3N), triphenylphosphine–diethyl azodicarboxylate (DEAD), ozone, dimethyl sulfide and [(methoxycarbonyl)methylene]triphenylphosphorane afforded a mixture of the (2*E*)- and (2*Z*)-enoate **31** and **32**. By a palladium(0)-catalyzed reaction,[4] a mixture of **31** and **32** was converted into the *cis*-(*E*)-enoate **31** (for details, see Experimental section). Likewise, the allyl alcohol **33**, which was previously synthesized,[4] was treated successively with TFA, Mts-Cl–Et_3N, Ph_3P–DEAD, ozone, dimethyl sulfide, [(benzyloxycarbonyl)methylene]triphenylphosphorane and $Pd(PPh_3)_4$ to give the *cis*-(*E*)-enoate **36**. N^{ε}-2-Chlorophenylmethoxycarbonyl (Cl-Z)-protected Lys **37** was also successively treated with Mts-Cl–Et_3N, 1-hydroxybenzotriazole (HOBt)–3-[3-(dimethylamino)propyl]-1-ethylcarbodiimide (WSCD)–*N*,*O*-dimethylhydroxylamine hydrochloride, DIBAL, vinylmagnesium chloride, Ph_3P–DEAD, ozone, dimethyl sulfide, [(benzyloxycarbonyl)methylene]triphenylphosphorane and $Pd(PPh_3)_4$ to yield the *cis*-(*E*)-enoate **44**. *N*-Boc-(*S*)-serinal acetonide **45** was successively treated with vinylmagnesium chloride, TFA–H_2O, Mts-Cl–DIPEA, benzyl bromide–sodium hydride and Ph_3P–DEAD to give a diastereomixture of vinylaziridines **52** and **53**. Reaction of the mixture of **52** and **53** with ozone, dimethyl sulfide, *N*-methyl(diethylphosphono)acetamide–DIPEA and $Pd(PPh_3)_4$ gave the *cis*-(*E*)-enamide **54**. Likewise, reaction of the mixture of **52** and **53** with ozone, dimethyl sulfide, [(methoxycarbonyl)methylene]triphenylphosphorane and $Pd(PPh_3)_4$ gave the *cis*-(*E*)-enoate **55**. The configuration of the γ- and δ-carbon centers and the (*E*)-stereochemistry for the double bonds in the above *N*-Mts-γ,δ-epimino α,β-enoates (enamide) were assigned on the basis of the NOE data and the coupling constants by NMR analyses.[5]

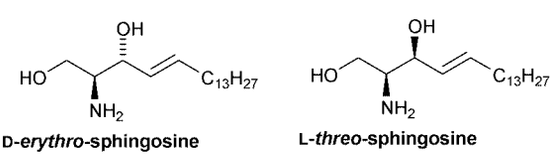
Synthesis of (*E*)-alkene dipeptide isosteres using the ring-opening reaction with MSA

We examined the feasibility of the stereoselective synthesis of (*E*)-alkene dipeptide isosteres by treatment of the ring-opened products with organocopper reagents. Treatment of the above mesyl compound **11**, which was prepared from the *cis*-(*E*)-enoate **10** by the MSA-mediated ring-opening reaction, with $BnCu(CN)MgCl{\cdot}BF_3$ (4 equiv.) in THF at −78 °C for 30 min yielded the protected (L-amino acid, D-amino acid)-type (2*S*,5*S*) dipeptide isostere, Mts-L-Val-ψ[(*E*)-CH=CH]-D-Phe-OMe, **56** in 94% yield based on **10** (diastereoselection > 99:1 from NMR analysis). This reaction occurred by an *anti*-S_N2' mechanism as shown in Scheme 4. In contrast, an *anti*-S_N2' reaction of the *cis*-(*E*)-enoate **10** with BnCu(CN)MgCl·2LiCl (4 equiv.) in THF at −78 °C for 30 min afforded the L,L-type (2*R*,5*S*) isostere, Mts-L-Val-ψ[(*E*)-CH=CH]-L-Phe-OMe, **57** in 75% yield as shown in Scheme 4. The most important factor of the MSA-mediated ring-opening reactions is the inversion of configuration at the C-γ carbon *via* an S_N2 mechanism. Thus, *cis*-(*E*) enoates lead to *syn*-(*E*)-mesyl esters, which are converted into L,D-type isosteres upon treatment with organocopper reagents. On the other hand, *cis*-(*E*)-enoates themselves produce L,L-type isosteres with organocopper reagents. In a comparative experiment, the *trans*-(*E*)-enoate **14** was treated with MSA to afford the *anti*-(*E*)-mesyl compound **15**, which was converted into the L,L-type isostere **57** with the organocopper reagent in 89% yield based on **14**. In contrast, treatment of the *trans*-(*E*)-enoate **14** with the organocopper reagent afforded the L,D-type isostere **56** in 77% yield. Taken together, two types of isosteres were stereoselectively synthesized from either the *cis*- or *trans*-(*E*)-enoate.

We evaluated the applicability of this synthetic methodology to diverse aziridine *cis*-(*E*)-enoates, such as D-amino acid-derived aziridines and aziridines bearing other functional groups. In the same manner as described above, the *cis*-(*E*)-enoate **31**, which was derived from D-Phe, afforded the corresponding D,L-type isostere, Mts-D-Phe-ψ[(*E*)-CH=CH]-L-Leu-OMe, **59** or the D,D-type isostere, Mts-D-Phe-ψ[(*E*)-CH=CH]-D-Leu-OMe, **60** by treatment with MSA and $Bu^iCu(CN)MgCl{\cdot}BF_3$ or $Bu^iCu(CN)MgCl{\cdot}2LiCl$, respectively. The benzyl ester-bearing aziridine **36** gave the corresponding L,D-type isostere, Mts-L-Leu-ψ[(*E*)-CH=CH]-D-Phe-OBn, **62** or the L,L-type isostere, Mts-L-Leu-ψ[(*E*)-CH=CH]-L-Phe-OBn, **63** in a similar manner using MSA and $BnCu(CN)MgCl{\cdot}BF_3$ or $BnCu(CN)MgCl{\cdot}2LiCl$, respectively. The *cis*-(*E*)-enoate **44** derived from L-lysine, which possesses the N^{ε}-(Cl-Z)-protected amino group and the benzyl ester group, was also converted into the isostere, Mts-L-Lys(Cl-Z)-ψ[(*E*)-CH=CH]-D-Ala-OBn, **65** or Mts-L-Lys(Cl-Z)-ψ[(*E*)-CH=CH]-L-Ala-OBn, **66** by treatment with MSA and $MeCu(CN)Li{\cdot}LiBr{\cdot}BF_3$ or $MeCu(CN)Li{\cdot}LiBr{\cdot}2LiCl$, respectively. The *cis*-(*E*)-enamide **54** derived from L-serine, which possesses the benzyl ether group and the *N*-methyl amide group, afforded the corresponding amide-type isostere, Mts-L-Ser(*O*-Bn)-ψ[(*E*)-CH=CH]-D-Ala-NHMe, **68** or Mts-L-Ser(*O*-Bn)-ψ[(*E*)-CH=CH]-L-Ala-NHMe, **69** by treatment with MSA and $MeCu(CN)Li{\cdot}LiBr{\cdot}BF_3$ or $MeCu(CN)Li{\cdot}LiBr{\cdot}2LiCl$, respectively. These results suggest that this synthetic method is widely applicable to various aziridinyl *cis*-(*E*)-enoates and enamides. The (*E*)-geometry of the double bond in the obtained isosteres **56**, **57**, **59**, **60**, **62**, **63**, **65**, **66**, **68** and **69** was assigned on the basis of the coupling constant of the two olefinic protons by ^{1}H-NMR analyses. The absolute configuration of the α-alkylated carbon centers in the above isosteres was well characterized by circular dichroism (CD) measurements.[5,6]

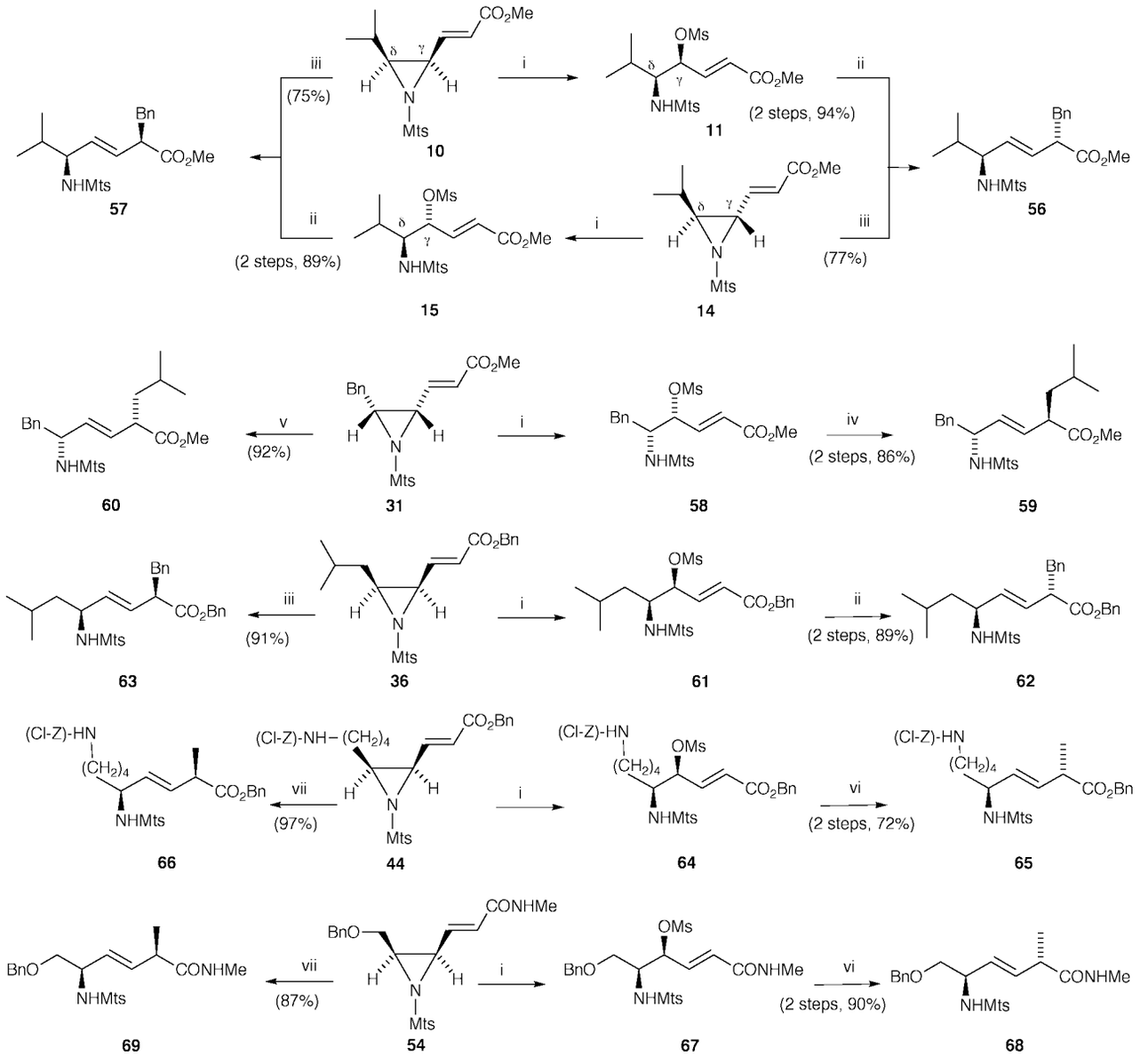
Synthesis of a key intermediate compound for the preparation of sphingosines using the ring-opening reaction with TFA

The sphingosines are important constituents of cell membranes, which participate in cell recognition phenomena such as growth, differentiation and immune responses. The sphingosines **72** and **73** are long-chain amino alcohols, and there have been many

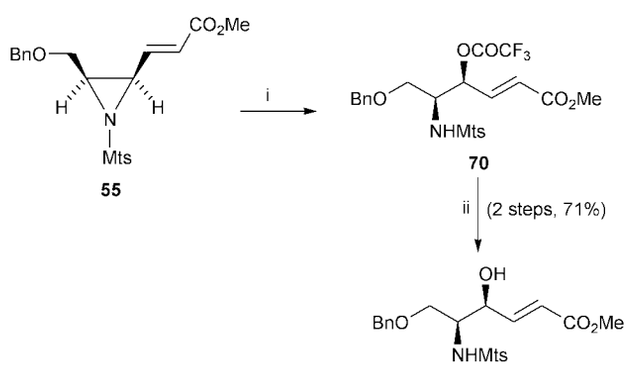


D-*erythro*-sphingosine **72** L-*threo*-sphingosine **73**

reports on their syntheses.[10b,14] One important factor in the asymmetric synthesis of D-*erythro*- and L-*threo*-sphingosine **72** and **73** is the stereocontrol in the preparation of the 1,2-amino alcohol. We investigated the feasibility of the stereocontrolled preparation of a key intermediate compound for the sphingosine synthesis using the TFA-mediated ring-opening reaction of a β-aziridinyl α,β-enoate. Exposure of the enoate **55** to TFA at rt for 15 h afforded δ-aminated γ-trifluoroacetoxy α,β-enoate **70** by the regiospecific S_N2 ring-opening reaction. The following hydrolysis of **70** yielded the δ-aminated γ-hydroxy α,β-enoate **71** in 71% yield based on **55** (Scheme 5). The amino alcohol **71** is a key intermediate compound for the L-*threo*-sphingosine **73** synthesis, and can be also converted into D-*erythro*-sphingosine **72** by suitable replacement of the N^{α}-protecting group and inversion of stereochemistry of the γ-hydroxy group using the Mitsunobu reaction.[13] This result suggests that the TFA-mediated ring-opening reaction is useful for the convenient synthesis of the diastereomerically pure δ-aminated



Scheme 4 *Reagents*: i, CH_3SO_3H; ii, $BnCu(CN)MgCl{\cdot}BF_3$; iii, BnCu(CN)MgCl·2LiCl; iv, $Bu^iCu(CN)MgCl{\cdot}BF_3$; v, $Bu^iCu(CN)MgCl{\cdot}2LiCl$; vi, $MeCu(CN)Li{\cdot}LiBr{\cdot}BF_3$; vii, MeCu(CN)Li·LiBr·2LiCl.



Scheme 5 *Reagents and conditions*: i, TFA; ii, hydrolysis.

γ-hydroxy α,β-enoates as the key intermediates for several bioactive compounds.

In conclusion, regio- and stereo-specific ring-opening reactions of *N*-Mts-protected aziridines bearing α,β-unsaturated esters [*cis*-(*E*)- and *trans*-(*E*)-isomers] by MSA or TFA have been found. The MSA-mediated ring-opening reactions provide a useful approach to the stereoselective synthesis of both L,L-type (or D,D-type) and L,D-type (or D,L-type) (*E*)-alkene dipeptide isosteres from a single substrate of either a γ,δ-*cis*- or -*trans*-γ,δ-epimino (*E*)-α,β-unsaturated ester. L,D-Type and D,L-type (*E*)-alkene dipeptide isosteres are also of comparable use to L,L-type and D,D-type isosteres in the field of medicinal chemistry. γ,δ-Epimino α,β-unsaturated esters can be easily prepared as a mixture of the *cis*-(*E*)-, *cis*-(*Z*)-, *trans*-(*E*)- and *trans*-(*Z*)-isomers from the corresponding chiral amino aldehydes. Pd(0)-catalyzed equilibration reactions of various stereomers of γ,δ-epimino α,β-enoates could afford predominantly *cis*-(*E*)-isomers in high yields.[4] Upon treatment with organocopper reagents, these would exclusively provide L,L-type (or D,D-type) (*E*)-alkene isosteres. Based on the above results, brief MSA treatment of *cis*-(*E*)-γ,δ-epimino α,β-unsaturated esters, gives γ,δ-*syn*-δ-aminated γ-mesyloxy (*E*)-α,β-enoates, which can be converted into L,D-type (or D,L-type) (*E*)-alkene isosteres *via* organocopper–BF_3-mediated *anti*-S_N2' reactions. Taken together, the completely stereocontrolled synthetic process for L,L-type, L,D-type, D,D-type and D,L-type (*E*)-alkene dipeptide isosteres starting from L-amino acid or D-amino acid has been established. Furthermore, the TFA-mediated ring-opening reactions of *cis*-(*E*)-enoates have provided a useful methodology for the stereoselective synthesis of δ-aminated γ-hydroxy α,β-enoates such as a key intermediate compound for the sphingosine synthesis. Many of the existing method-

ologies for the synthesis of sphingosines are accompanied by difficulties in 1,2-amino alcohol stereocontrol.[10b,14] However, our procedure lacks such stereocontrol problems, since TFA-mediated stereoselective ring-opening reactions of β-aziridinyl α,β-enoates are unequivocally related to the stereochemistry of 1,2-amino alcohol construction.

Experimental

General

^{1}H NMR spectra were recorded using a JEOL EX-270 or a Bruker AC 300 spectrometer at 270 or 300 MHz ^{1}H frequency for samples in $CDCl_3$. Chemical shifts are reported in parts per million downfield from internal tetramethylsilane. Nominal (LRMS) and exact mass (HRMS) spectra were recorded on a JEOL JMS-01SG-2 or JMS-HX/HX 110A mass spectrometer. Optical rotations were measured in $CHCl_3$ with a JASCO DIP-360 digital polarimeter. CD spectra were measured in isooctane (2,2,4-trimethylpentane) at 24 °C with a JASCO J-720 spectropolarimeter. IR spectra were obtained on a Shimadzu Model IR-400 spectrometer. Mps were measured by a hot stage melting point apparatus and are uncorrected. For flash chromatography, silica gel 60 H (silica gel for thin-layer chromatography, Merck) and Wakogel C-200 (silica gel for column chromatography) were employed.

Reaction of methyl (2*E*,4*R*,5*S*)-6-methyl-4,5-[*N*-(2,4,6-trimethylphenylsulfonyl)epimino]hept-2-enoate 10 with MSA in $CHCl_3$

To a stirred solution of the *cis*-(*E*)-enoate **10** (151 mg, 0.430 mmol) in $CHCl_3$ (4.3 cm^3) was added dropwise MSA (0.279 cm^3, 4.30 mmol) at rt with stirring, and the stirring was continued for 20 min. The mixture was extracted with EtOAc and the extract was washed successively with 5% citric acid, water, 5% $NaHCO_3$ and water, and dried over $MgSO_4$. Concentration under reduced pressure gave the crude mesyl compound **11**, as a colourless oil (crude), δ_H(270 MHz; $CDCl_3$) 0.85 (3 H, d, *J* 6.6, CMe), 0.89 (3 H, d, *J* 6.6, CMe), 1.88 (1 H, m, 6-H), 2.29 (3 H, s, CMe), 2.66 (6 H, s, CMe), 3.02 (3 H, s, SMe), 3.40 (1 H, m, 5-H), 3.71 (3 H, s, OMe), 4.83 (1 H, d, *J* 9.6, NH), 5.27 (1 H, m, 4-H), 6.03 (1 H, dd, *J* 15.5 and 1.3, CH=), 6.72 (1 H, dd, *J* 15.5 and 6.0, CH=) and 6.93 (2 H, s, ArH); *m*/*z* (FAB-LRMS) 448 (MH^+), 446, 352, 254, 183, 167, 119 and 91 (base peak).

Reaction of methyl (2*E*,4*R*,5*S*)-6-methyl-4,5-[*N*-(2,4,6-trimethylphenylsulfonyl)epimino]hept-2-enoate 10 with TFA

The *cis*-(*E*)-enoate **10** (108 mg, 0.306 mmol) was dissolved in TFA (1 cm^3) at rt and the solution was stirred for 15 h. Concentration under reduced pressure gave a crude product **12** as an oil. Hydrolysis, and purification by flash chromatography over silica gel with *n*-hexane–EtOAc (4:1) afforded the hydrolysate **13** (106 mg, 0.236 mmol, 71% yield based on **10**) as a crystalline mass.

Compound **12**, colourless oil (crude), δ_H(270 MHz; $CDCl_3$) 0.89 (3 H, d, *J* 6.9, CMe), 0.96 (3 H, d, *J* 6.9, CMe), 1.83 (1 H, m, 6-H), 2.29 (3 H, s, CMe), 2.63 (6 H, s, CMe), 3.49 (1 H, m, 5-H), 3.68 (3 H, s, OMe), 4.80 (1 H, d, *J* 8.9, NH), 5.64 (1 H, m, 4-H), 5.77 (1 H, dd, *J* 15.8 and 1.7, CH=), 6.57 (1 H, dd, *J* 15.8 and 5.3, CH=) and 6.91 (2 H, s, ArH); *m*/*z* (FAB-LRMS) 488 (MNa^+), 466 (MH^+), 352, 254, 183, 167, 119 and 91 (base peak).

Compound **13**, colourless crystals, mp 157–158 °C [from *n*-hexane–Et_2O (3:1)] (Found: C, 58.51; H, 7.31; N, 3.73. $C_{18}H_{27}NO_5S$ requires C, 58.51; H, 7.37; N, 3.79%); $[\alpha]_D^{27}$ −42.1 (*c* 0.569 in $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 0.76 (3 H, d, *J* 6.6, CMe), 0.89 (3 H, d, *J* 6.9, CMe), 1.88 (1 H, m, 6-H), 2.28 (3 H, s, CMe), 2.62 (6 H, s, CMe), 2.69 (1 H, m, OH), 3.12 (1 H, m, 5-H), 3.69 (3 H, s, OMe), 4.33 (1 H, m, 4-H), 5.04 (1 H, m, NH), 5.94 (1 H, dd, *J* 15.5 and 1.7, CH=), 6.68 (1 H, dd, *J* 15.5 and 5.0, CH=) and 6.90 (2 H, s, ArH); *m*/*z* (FAB-LRMS) 392 (MNa^+), 370 (MH^+), 254, 183, 167, 119, 91 (base peak) and 72.

Methyl (2*E*,4*R*,5*S*)-6-methyl-4,5-[*N*-(2,4,6-trimethylphenylsulfonyl)epimino]hept-2-enoate 10 from 13 (confirmation of the γ,δ-*threo* stereochemistry of 13)

Ph_3P (13.4 mg, 0.0512 mmol) and DEAD (0.0202 cm^3 of a 40% solution in toluene, 0.0512 mmol) were added to a stirred solution of the alcohol **13** (17.2 mg, 0.0466 mmol) in 0.2 cm^3 of THF at 0 °C, and the mixture was stirred at this temperature for 30 min. The mixture was concentrated under reduced pressure to give an oil, which was purified by flash chromatography over silica gel with *n*-hexane–EtOAc (3:1) to yield 11.5 mg (0.0327 mmol, 70%) of *compound* **10**, colourless crystals, mp 76–78 °C [from *n*-hexane–Et_2O (3:1)] (Found: C, 61.26; H, 7.18; N, 3.91. $C_{18}H_{25}NO_4S$ requires C, 61.51; H, 7.17; N, 3.99%); $[\alpha]_D^{18}$ −78.0 (*c* 0.407 in $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 0.79 (3 H, d, *J* 6.6, CMe), 0.87 (3 H, d, *J* 6.9, CMe), 1.42 (1 H, m, 6-H), 2.31 (3 H, s, CMe), 2.66 (1 H, dd, *J* 10.2 and 7.3, 5-H), 2.70 (6 H, s, CMe), 3.48 (1 H, t, *J* 7.1, 4-H), 3.74 (3 H, s, OMe), 6.09 (1 H, dd, *J* 15.5 and 1.0, CH=), 6.72 (1 H, dd, *J* 15.5 and 6.6, CH=) and 6.96 (2 H, s, ArH).

Reaction of methyl (2*E*,4*S*,5*S*)-6-methyl-4,5-[*N*-(2,4,6-trimethylphenylsulfonyl)epimino]hept-2-enoate 14 with MSA in $CHCl_3$

By use of a procedure similar to that described for the preparation of **11** from **10**, the *trans*-(*E*)-enoate **14** (120 mg, 0.342 mmol) was converted into the γ-mesyloxy-α,β-enoate **15** (colourless oil) by treatment with MSA in $CHCl_3$.

Compound **15**, colourless oil (crude), δ_H(270 MHz; $CDCl_3$) 0.79 (3 H, d, *J* 6.9, CMe), 0.93 (3 H, d, *J* 6.9, CMe), 1.85 (1 H, m, 6-H), 2.30 (3 H, s, CMe), 2.64 (6 H, s, CMe), 2.92 (3 H, s, SMe), 3.40 (1 H, m, 5-H), 3.76 (3 H, s, OMe), 4.80 (1 H, d, *J* 9.6, NH), 5.35 (1 H, m, 4-H), 6.07 (1 H, dd, *J* 15.8 and 1.7, CH=), 6.80 (1 H, dd, *J* 15.8 and 5.6, CH=) and 6.96 (2 H, s, ArH); *m*/*z* (FAB-LRMS) 448 (MH^+), 446, 352, 254, 183 (base peak) and 119.

Reaction of methyl (2*E*,4*S*,5*S*)-6-methyl-4,5-[*N*-(2,4,6-trimethylphenylsulfonyl)epimino]hept-2-enoate 14 with TFA

By use of a procedure similar to that described for the preparation of **12** from **10**, the *trans*-(*E*)-enoate **14** (139 mg, 0.396 mmol) was converted into the γ-trifluoroacetoxy-α,β-enoate **16** (colourless oil) by treatment with TFA. Hydrolysis, and purification by flash chromatography gave the hydrolysate **17** (133.3 mg, 0.361 mmol, 91% yield) as a colourless oil.

Compound **16**, colourless oil (crude), δ_H(270 MHz; $CDCl_3$) 0.83 (3 H, d, *J* 6.6, CMe), 0.87 (3 H, d, *J* 7.0, CMe), 1.85 (1 H, m, 6-H), 2.30 (3 H, s, CMe), 2.59 (6 H, s, CMe), 3.51 (1 H, m, 5-H), 3.77 (3 H, s, OMe), 4.97 (1 H, d, *J* 9.5, NH), 5.53 (1 H, m, 4-H), 5.98 (1 H, dd, *J* 15.5 and 1.3, CH=), 6.78 (1 H, dd, *J* 15.8 and 5.6, CH=) and 6.94 (2 H, s, ArH); *m*/*z* (FAB-LRMS) 466 (MH^+), 352, 290, 254, 183, 167, 119, 91 (base peak) and 72.

Compound **17**, colourless oil [Found (FAB): $(M + H)^+$, 370.1693. $C_{18}H_{27}NO_5S$ requires *M* + H, 370.1688]; $[\alpha]_D^{25}$ −58.9 (*c* 1.0 in $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 0.73 (3 H, d, *J* 6.6, CMe), 0.78 (3 H, d, *J* 7.0, CMe), 1.70 (1 H, m, 6-H), 2.30 (3 H, s, CMe), 2.64 (6 H, s, CMe), 3.06 (1 H, m, OH), 3.15 (1 H, m, 5-H), 3.75 (3 H, s, OMe), 4.51 (1 H, m, 4-H), 4.97 (1 H, m, NH), 6.16 (1 H, dd, *J* 15.5 and 1.7, CH=), 6.91 (1 H, dd, *J* 15.5 and 4.0, CH=) and 6.96 (2 H, s, ArH); *m*/*z* (FAB-LRMS) 392 (MNa^+), 370 (MH^+), 352, 254, 183, 167, 119, 91 (base peak) and 72.

Methyl (2*E*,4*S*,5*S*)-6-methyl-4,5-[*N*-(2,4,6-trimethylphenylsulfonyl)epimino]hept-2-enoate 14 from 17 (confirmation of the γ,δ-*erythro* stereochemistry of 17)

By use of a procedure similar to that described for the prepar-

ation of **10** from **13**, the alcohol **17** (32.0 mg, 0.0866 mmol) was converted into the *trans*-(*E*)-enoate **14** (20.8 mg, 0.0592 mmol, 68%) colourless crystals, mp 107–108 °C (from *n*-hexane) [Found (FAB): $(M + H)^+$, 352.1588. $C_{18}H_{25}NO_4S$ requires $M + H$, 352.1582]; $[\alpha]_D^{26}$ −11.0 (*c* 1.09 in $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 0.76 (3 H, d, *J* 6.9, CMe), 0.89 (3 H, d, *J* 6.6, CMe), 1.56 (1 H, m, 6-H), 2.30 (3 H, s, CMe), 2.69 (6 H, s, CMe), 2.90 (1 H, dd, *J* 7.6 and 4.0, 5-H), 3.14 (1 H, dd, *J* 10.2 and 4.0, 4-H), 3.75 (3 H, s, OMe), 6.13 (1 H, d, *J* 15.5, CH=), 6.94 (2 H, s, ArH) and 7.16 (1 H, dd, *J* 15.5 and 10.2, CH=); *m*/*z* (FAB-LRMS) 374 (MNa^+), 352 (MH^+), 320, 296 (base peak), 183, 168, 137 and 119.

Methyl (2*E*)-3-[(4*S*,5*S*)-2,2-dimethyl-4-methylethyl-*N*-(2,4,6-trimethylphenylsulfonyl)oxazolidin-5-yl]prop-2-enoate 20

To a stirred solution of 149 mg (0.402 mmol) of **13** in a mixture of 3 cm^3 of toluene and 0.148 cm^3 (1.21 mmol) of 2,2-dimethoxypropane at rt was added 1.52 mg (6.03 μmol) of pyridinium toluene-*p*-sulfonate, and the mixture was gently refluxed for 3 h. The mixture was made alkaline with saturated $NaHCO_3$ solution and extracted with Et_2O. The extract was washed with water and dried over $MgSO_4$. Concentration under reduced pressure gave a crystalline residue, which was flash chromatographed over silica gel with *n*-hexane–EtOAc (3:1) to yield 139 mg (0.339 mmol, 84%) of *compound* **20** as colourless crystals, mp 128–129 °C [from *n*-hexane–Et_2O (3:1)] (Found: C, 61.48; H, 7.46; N, 3.39. $C_{21}H_{31}NO_5S$ requires C, 61.59; H, 7.63; N, 3.42%); $[\alpha]_D^{28}$ −115.6 (*c* 1.33 in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 0.63 (3 H, d, *J* 6.6, CMe), 0.68 (3 H, d, *J* 6.9, CMe), 0.93 (1 H, m, 5-H), 1.81 (3 H, s, CMe), 1.84 (3 H, s, CMe), 2.36 (3 H, s, CMe), 2.69 (6 H, s, CMe), 3.78 (1 H, t, *J* 3.8, 4-H), 3.81 (3 H, s, OMe), 4.59 (1 H, m, 3-H), 6.07 (1 H, dd, *J* 15.7 and 1.7, CH=), 7.00 (2 H, s, ArH) and 7.08 (1 H, dd, *J* 15.7 and 4.8, CH=).

Methyl (2*E*)-3-[(4*S*,5*R*)-2,2-dimethyl-4-methylethyl-*N*-(2,4,6-trimethylphenylsulfonyl)oxazolidin-5-yl]prop-2-enoate 21

By use of a procedure similar to that described for the preparation of **20** from **13**, the alcohol **17** (120 mg, 0.326 mmol) was converted into the oxazolidinyl derivative **21** (86.2 mg, 0.211 mmol, 65%) as a colourless oil [Found (FAB): $(M + H)^+$, 410.1994. $C_{21}H_{31}NO_5S$ requires $M + H$, 410.2001]; $[\alpha]_D^{28}$ −46.8 (*c* 1.24 in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 0.60 (3 H, d, *J* 7.1, CMe), 0.65 (3 H, d, *J* 6.9, CMe), 0.89 (1 H, m, 5-H), 1.83 (3 H, s, CMe), 1.91 (3 H, s, CMe), 2.34 (3 H, s, CMe), 2.70 (6 H, s, CMe), 3.68 (1 H, dd, *J* 5.7 and 3.8, 4-H), 3.78 (3 H, s, OMe), 4.92 (1 H, m, 3-H), 6.21 (1 H, dd, *J* 15.6 and 1.8, CH=), 6.99 (2 H, s, ArH) and 7.08 (1 H, dd, *J* 15.7 and 4.5, CH=); *m*/*z* (FAB-LRMS) 410 (MH^+), 366, 240, 183, 119 and 112 (base peak).

Reaction of methyl (2*Z*,4*R*,5*S*)-6-methyl-4,5-[*N*-(2,4,6-trimethylphenylsulfonyl)epimino]hept-2-enoate 18 with MSA in $CHCl_3$ and production of (4*S*,5*S*)-6-methyl-5-(2,4,6-trimethylphenylsulfonylamino)hept-2-en-4-olide 22

By use of a procedure similar to that described for the reaction of **10** with MSA in $CHCl_3$, the *cis*-(*Z*)-enoate **18** (238 mg, 0.675 mmol) was treated with MSA (6.08 mmol) in $CHCl_3$ to yield complex mixtures containing the γ-lactone ring-cyclized product **22** (59 mg, 0.175 mmol, 26%), which was purified by flash chromatography over silica gel with *n*-hexane–EtOAc (4:1).

Compound **22**, colourless crystals, mp 217–218 °C [from *n*-hexane–EtOAc (5:1)] (Found: C, 60.26; H, 6.66; N, 4.11. $C_{17}H_{23}NO_4S$ requires C, 60.53; H, 6.82; N, 4.15%); $[\alpha]_D^{19}$ −181.4 (*c* 2.69 in $CHCl_3$); IR ($CHCl_3$) 3410, 3240, 2960, 1752, 1600, 1455, 1408, 1327, 1158, 1100, 1071, 1057, 1028, 910, 850, 815, 650 cm^{-1}; δ_H(270 MHz; $CDCl_3$) 0.87 (3 H, d, *J* 6.6, CMe), 0.97 (3 H, d, *J* 6.9, CMe), 1.93 (1 H, m, 6-H), 2.30 (3 H, s, CMe), 2.64 (6 H, s, CMe), 3.43 (1 H, m, 5-H), 4.64 (1 H, d, *J* 9.6, NH), 5.15 (1 H, m, 4-H), 5.86 (1 H, dd, *J* 5.6 and 2.0, CH=), 6.94 (2 H, s, ArH) and 7.11 (1 H, dd, *J* 5.6 and 1.3, CH=); *m*/*z* (FAB-LRMS) 338 (MH^+), 254, 183 (base peak), 154, 137 and 119.

Reaction of methyl (2*Z*,4*R*,5*S*)-6-methyl-4,5-[*N*-(2,4,6-trimethylphenylsulfonyl)epimino]hept-2-enoate 18 with TFA

By use of a procedure similar to that described for the reaction of **10** with TFA, the *cis*-(*Z*)-enoate **18** (146 mg, 0.415 mmol) was treated with TFA to afford an inseparable complex mixture.

Reaction of methyl (2*Z*,4*S*,5*S*)-6-methyl-4,5-[*N*-(2,4,6-trimethylphenylsulfonyl)epimino]hept-2-enoate 19 with MSA in $CHCl_3$ and production of (4*R*,5*S*)-6-methyl-5-(2,4,6-trimethylphenylsulfonylamino)hept-2-en-4-olide 23

By use of a procedure similar to that described for the reaction of **10** with MSA in $CHCl_3$, the *trans*-(*Z*)-enoate **19** (256 mg, 0.727 mmol) was treated with MSA (6.55 mmol) in $CHCl_3$ to yield complex mixtures containing the γ-lactone ring-cyclized product **23** (142 mg, 0.419 mmol, 58%), which was purified by flash chromatography over silica gel with *n*-hexane–EtOAc (4:1).

Compound **23**, colourless oil [Found (FAB): $(M - H)^-$, 336.1279. $C_{17}H_{23}NO_4S$ requires $M - H$, 336.1269]; $[\alpha]_D^{24}$ +72.6 (*c* 0.36 in $CHCl_3$); IR ($CHCl_3$) 3290, 2980, 2360, 1720, 1594, 1499, 1412, 1368, 1328, 1199, 1150, 1108, 1074, 1037, 918, 870, 846, 715, 660 cm^{-1}; δ_H(270 MHz; $CDCl_3$) 0.76 (3 H, d, *J* 6.9, CMe), 0.94 (3 H, d, *J* 6.9, CMe), 1.90 (1 H, m, 6-H), 2.33 (3 H, s, CMe), 2.65 (6 H, s, CMe), 4.00 (1 H, m, 5-H), 4.03 (1 H, m, 4-H), 4.83 (1 H, d, *J* 9.6, NH), 5.99 (1 H, dd, *J* 9.6 and 1.7, CH=), 6.60 (1 H, ddd, *J* 9.6, 3.3 and 0.7, CH=) and 7.00 (2 H, s, ArH); *m*/*z* (FAB-LRMS) 338 (MH^+), 254, 183 (base peak), 149, 119 and 115.

Reaction of methyl (2*Z*,4*S*,5*S*)-6-methyl-4,5-[*N*-(2,4,6-trimethylphenylsulfonyl)epimino]hept-2-enoate 19 with TFA and production of (4*R*,5*S*)-6-methyl-5-(2,4,6-trimethylphenylsulfonylamino)hept-2-en-4-olide 23

By use of a procedure similar to that described for the reaction of **10** with TFA, the *trans*-(*Z*)-enoate **19** (130 mg, 0.370 mmol) was treated with TFA (1 cm^3) to yield complex mixtures containing the γ-lactone ring-cyclized product **23** (14.4 mg, 0.0427 mmol, 12%), which was purified by flash chromatography over silica gel with *n*-hexane–EtOAc (4:1).

Compound **23**, colourless oil [Found (FAB): $(M - H)^-$, 336.1268. $C_{17}H_{23}NO_4S$ requires $M - H$, 336.1270]; $[\alpha]_D^{24}$ +69.4 (*c* 0.42 in $CHCl_3$); IR ($CHCl_3$) 3350, 2990, 2370, 1720, 1595, 1500, 1414, 1366, 1335, 1202, 1148, 1108, 1074, 1038, 920, 870, 842, 715, 664 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 0.76 (3 H, d, *J* 6.8, CMe), 0.94 (3 H, d, *J* 6.9, CMe), 1.90 (1 H, m, 6-H), 2.33 (3 H, s, CMe), 2.64 (6 H, s, CMe), 3.97 (1 H, m, 5-H), 3.99 (1 H, m, 4-H), 4.98 (1 H, d, *J* 9.4, NH), 5.98 (1 H, dd, *J* 9.8 and 1.7, CH=), 6.59 (1 H, ddd, *J* 9.8, 3.2 and 0.7, CH=) and 7.00 (2 H, s, ArH); *m*/*z* (FAB-LRMS) 336 [$(M - H)^-$], 198 (base peak), 183, 153 and 151.

(*R*)-*N*-(*tert*-Butoxycarbonyl)phenylalaninol 25

DIBAL in *n*-hexane (73.8 cm^3, 68.6 mmol; 0.93 mol dm^{-3} solution) was added dropwise to a stirred solution of the ester **24** (5 g, 17.9 mmol) in 20 cm^3 of CH_2Cl_2 at −78 °C under argon. The mixture was allowed to warm to rt and stirring was continued for 3 h. The mixture was recooled to −78 °C, and saturated aq. NH_4Cl (10 cm^3) was added dropwise with vigorous stirring. The inorganic salts were removed by filtration through Celite. The filtrate was extracted with EtOAc, and the extract was washed with water and dried over $MgSO_4$. The usual work-up and flash chromatography over silica gel with *n*-hexane–EtOAc (2:1) gave a crystalline mass. Recrystallization from *n*-hexane–EtOAc (3:1) gave 3.27 g (13.0 mmol,

73%) of the *title compound* **25** as colourless crystals, mp 99 °C [from *n*-hexane–EtOAc (3:1)] (Found: C, 66.74; H, 8.30; N, 5.53. $C_{14}H_{21}NO_3$ requires C, 66.90; H, 8.42; N, 5.57%); $[\alpha]_D^{20}$ +22.9 (*c* 1.41 in $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.41 (9 H, s, CMe), 2.53 (1 H, m, OH), 2.84 (2 H, d, *J* 6.8, CH_2), 3.55 (1 H, m, C*H*H), 3.64 (1 H, m, CH*H*), 3.86 (1 H, m, CH), 4.81 (1 H, m, NH) and 7.19–7.33 (5 H, m, Ph).

(3*R*,4*R*)-4-[(*tert*-Butoxycarbonylamino)-5-phenylpent-1-en-3-ol 27 and (3*S*,4*R*)-4-(*tert*-butoxycarbonylamino)-5-phenylpent-1-en-3-ol 28

To a stirred solution of oxalyl dichloride (6.54 cm^3, 75 mmol) in dry CH_2Cl_2 (70 cm^3) at −78 °C under argon was added dropwise a solution of DMSO (11.7 cm^3, 165 mmol) in CH_2Cl_2 (20 cm^3). After 20 min, a solution of the alcohol **25** (12.6 g, 50 mmol) in CH_2Cl_2 (20 cm^3) was added to the above reagent at −78 °C, and the mixture was stirred for 1 h. DIPEA (52.3 cm^3, 300 mmol) was added dropwise to the above mixture at −78 °C, and the mixture was stirred for 2 h with warming to 0 °C. The reaction was quenched with 20 cm^3 of saturated aq. NH_4Cl at −78 °C with vigorous stirring. The mixture was extracted with Et_2O and the extract was washed successively with 5% citric acid, water, 5% $NaHCO_3$ and water, and dried over $MgSO_4$. Concentration under reduced pressure gave the crude aldehyde **26** as a colourless oil. To a stirred solution of $ZnCl_2$ (27.3 g, 200 mmol) and LiCl (17.0 g, 400 mmol) in 200 cm^3 of Et_2O at −78 °C was added *via* syringe 97.6 cm^3 (200 mmol) of 2.05 mol dm^{-3} vinylmagnesium chloride in THF. After being stirred at this temperature for 10 min, a solution of the above crude aldehyde **26** in THF (50 cm^3) was added dropwise to the mixture, and the mixture was allowed to warm to −40 °C and stirred at this temperature for 4 h, followed by quenching with 100 cm^3 of aq. 0.05 mol dm^{-3} HCl. The mixture was concentrated under reduced pressure and extracted with EtOAc. Usual work-up led to a mixture of products as a colourless oil, which was separated by flash chromatography over silica gel eluting with *n*-hexane–EtOAc (5:1), yielding, in order of elution, **27** (6.31 g, 22.8 mmol, 46%) and **28** (1.05 g, 3.79 mmol, 8%).

Compound **27**, colourless crystals, mp 93–96 °C [from *n*-hexane–Et_2O (3:1)] (Found: C, 69.12; H, 8.46; N, 5.04. $C_{16}H_{23}NO_3$ requires C, 69.30; H, 8.36; N, 5.05%); $[\alpha]_D^{20}$ +52.6 (*c* 0.966 in $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.38 (9 H, s, CMe), 2.30 (1 H, m, OH), 2.92 (2 H, m, CH_2), 3.80 (1 H, m, 4-H), 4.11 (1 H, m, 3-H), 4.77 (1 H, m, NH), 5.19 (1 H, ddd, *J* 10.2, 1.3 and 1.3, C*H*H=), 5.28 (1 H, ddd, *J* 17.2, 1.3 and 1.3, CH*H*=), 5.90 (1 H, ddd, *J* 17.2, 10.6 and 5.6, CH=) and 7.18–7.34 (5 H, m, Ph).

Compound **28**, colourless crystals, mp 120–122 °C [from *n*–hexane–Et_2O (3:1)] (Found: C, 69.26; H, 8.56; N, 5.02. $C_{16}H_{23}NO_3$ requires C, 69.30; H, 8.36; N, 5.05%); $[\alpha]_D^{20}$ +25.5 (*c* 0.964 in $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.36 (9 H, s, CMe), 2.73 (1 H, dd, *J* 13.9 and 8.9, C*H*H), 2.85 (1 H, dd, *J* 14.2 and 5.3, CH*H*), 2.96 (1 H, m, OH), 3.97 (1 H, m, 4-H), 4.24 (1 H, m, 3-H), 4.56 (1 H, m, NH), 5.29 (1 H, ddd, *J* 10.6, 1.3 and 1.3, C*H*H=), 5.37 (1 H, ddd, *J* 17.2, 1.3 and 1.3, CH*H*=), 5.94 (1 H, ddd, *J* 17.2, 10.6 and 5.6, CH=) and 7.18–7.42 (5 H, m, Ph).

(3*R*,4*R*)-5-Phenyl-4-(2,4,6-trimethylphenylsulfonylamino)pent-1-en-3-ol 29

TFA (5 cm^3) and anisole (0.969 cm^3, 8.97 mmol) were added to 2.49 g (8.97 mmol) of the alcohol **27** at 0 °C, and the mixture was stirred for 2 h. The mixture was concentrated under reduced pressure to give an oily residue, which was washed with *n*-hexane. To the oil in 5 cm^3 of $CHCl_3$ were added at 0 °C successively 3.7 cm^3 (26.9 mmol) of Et_3N and 2.35 g (10.8 mmol) of Mts-Cl. After being stirred for 15 h, the mixture was made acidic with saturated aq. citric acid and extracted with EtOAc, and the extract was washed with water and dried over $MgSO_4$. Purification by flash chromatography over silica gel with *n*-hexane–EtOAc (3:1) gave 2.12 g (5.91 mmol, 66%) of the *title compound* **29** as colourless crystals, mp 95–97 °C [from *n*-hexane–Et_2O (3:1)] (Found: C, 66.65; H, 6.97; N, 3.82. $C_{20}H_{25}NO_3S$ requires C, 66.82; H, 7.01; N, 3.90%); $[\alpha]_D^{27}$ +42.4 (*c* 0.932 in $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.99 (1 H, d, *J* 3.6, OH), 2.28 (3 H, s, CMe), 2.56 (6 H, s, CMe), 2.67 (1 H, dd, *J* 13.5 and 6.3, C*H*H), 2.94 (1 H, dd, *J* 13.5 and 8.3, CH*H*), 3.44 (1 H, m, 4-H), 4.11 (1 H, m, 3-H), 4.96 (1 H, d, *J* 8.6, NH), 5.09 (1 H, m, C*H*H=), 5.21 (1 H, m, CH*H*=), 5.69 (1 H, ddd, *J* 17.2, 10.6 and 5.9, CH=), 6.87 (2 H, s, ArH) and 7.00–7.18 (5 H, m, Ph).

(2*R*,3*S*)-2-Benzyl-*N*-(2,4,6-trimethylphenylsulfonyl)-3-vinylaziridine 30

Ph_3P (0.950 g, 3.62 mmol) and DEAD (0.570 cm^3 of a 40% solution in toluene, 3.62 mmol) were added to a stirred solution of the alcohol **29** (1.18 g, 3.29 mmol) in 3 cm^3 of THF at 0 °C, and the mixture was stirred at this temperature for 30 min. The mixture was concentrated under reduced pressure to give an oil, which was purified by flash chromatography over silica gel with *n*-hexane–EtOAc (3:1) to yield 1.11 g (3.26 mmol, 99%) of *compound* **30** as colourless crystals, mp 72–73 °C [from *n*-hexane–Et_2O (3:1)] (Found: C, 70.20; H, 6.82; N, 3.96. $C_{20}H_{23}NO_2S$ requires C, 70.35; H, 6.79; N, 4.10%); $[\alpha]_D^{27}$ +26.2 (*c* 0.910 in $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 2.28 (3 H, s, CMe), 2.58 (6 H, s, CMe), 2.64 (1 H, dd, *J* 14.5 and 7.6, C*H*H), 2.75 (1 H, dd, *J* 14.5 and 5.6, CH*H*), 3.09 (1 H, ddd, *J* 7.6, 7.6 and 5.6, 2-H), 3.47 (1 H, m, 3-H), 5.37 (1 H, m, C*H*H=), 5.50 (1 H, m, CH*H*=), 5.78 (1 H, ddd, *J* 16.8, 10.6 and 6.6, CH=), 6.84 (2 H, s, ArH) and 6.94–7.14 (5 H, m, Ph).

Methyl (2*E*,4*S*,5*R*)-6-phenyl-4,5-[*N*-(2,4,6-trimethylphenylsulfonyl)epimino]hex-2-enoate 31

O_3 was bubbled through a solution of the vinylaziridine **30** (1.02 g, 2.98 mmol) in 15 cm^3 of MeOH–$CHCl_3$ (3:1) at −78 °C until a blue colour persisted. Nitrogen was bubbled through the solution with stirring for 30 min during which time it was allowed to warm to 0 °C. To the solution at 0 °C was added dimethyl sulfide (0.240 cm^3, 3.28 mmol), and the mixture was stirred for 30 min. Concentration under reduced pressure left an oily residue, which was dissolved in $CHCl_3$ (10 cm^3). To the mixture at 0 °C was added [(methoxycarbonyl)methylene]-triphenylphosphorane (1.99 g, 5.96 mmol), and the mixture was stirred for 2 h. The mixture was concentrated under reduced pressure to leave a semisolid, which was extracted with EtOAc and the extract was washed successively with 1 mol dm^{-3} HCl, water, saturated aq. $NaHCO_3$ and water, and dried over $MgSO_4$. Concentration under reduced pressure gave a residue, which was purified by flash chromatography over silica gel with *n*-hexane–EtOAc (5:1) to give a mixture of the enoates **31** and **32**, which was dissolved in 10 cm^3 of dry THF, and to the mixture at 0 °C under argon was added by syringe with stirring a solution of $Pd(PPh_3)_4$ (147 mg, 0.128 mmol, 5 mol%) in 5 cm^3 of dry THF. After 4 h, the mixture was allowed to warm to rt, and the stirring was continued for a further 15 h. Purification by flash chromatography over silica gel with *n*-hexane–EtOAc (5:1) and recrystallization from *n*-hexane gave 577 mg (1.44 mmol, 57% yield based on **30**) of the cis-(*E*)-*enoate* **31** as colourless crystals, mp 54–55 °C (from *n*-hexane) (Found: C, 65.99; H, 6.24; N, 3.49. $C_{22}H_{25}NO_4S$ requires C, 66.14; H, 6.31; N, 3.51%); $[\alpha]_D^{19}$ +64.9 (*c* 0.575 in $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 2.30 (3 H, s, CMe), 2.57 (6 H, s, CMe), 2.64 (1 H, dd, *J* 14.6 and 8.4, C*H*H), 2.76 (1 H, dd, *J* 14.6 and 5.1, CH*H*), 3.19 (1 H, m, 5-H), 3.56 (1 H, m, 4-H), 3.77 (3 H, s, OMe), 6.20 (1 H, dd, *J* 15.8 and 1.0, CH=), 6.85 (1 H, dd, *J* 15.8 and 6.6, CH=), 6.86 (2 H, s, ArH) and 6.92–7.12 (5 H, m, Ph); *m*/*z* (FAB-LRMS) 400 (MH^+), 216, 183 (base peak), 119 and 91.

(3*S*,4*S*)-6-Methyl-4-(2,4,6-trimethylphenylsulfonylamino)hept-1-en-3-ol 34

By use of a procedure identical with that described for the preparation of **29** from **27**, the known alcohol **33** (3.63 g, 14.9 mmol) was converted into 3.99 g (12.3 mmol, 82%) of the *title compound* **34**, as colourless crystals, mp 137–138 °C [from *n*-hexane–Et_2O (3:1)] (Found: C, 62.77; H, 8.45; N, 4.27. $C_{17}H_{27}NO_3S$ requires C, 62.74; H, 8.36; N, 4.30%); $[\alpha]_D^{25}$ −14.1 (*c* 0.951 in $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 0.69 (3 H, d, *J* 6.3, CMe), 0.78 (3 H, d, *J* 6.6, CMe), 1.23 (1 H, m, C*H*H), 1.40 (1 H, m, CH*H*), 1.44 (1 H, m, 6-H), 2.07 (1 H, d, *J* 4.0, OH), 2.30 (3 H, s, CMe), 2.63 (6 H, s, CMe), 3.29 (1 H, m, 4-H), 4.05 (1 H, m, 3-H), 4.75 (1 H, d, *J* 9.2, NH), 5.07 (1 H, m, C*H*H=), 5.20 (1 H, m, CH*H*=), 5.68 (1 H, ddd, *J* 17.2, 10.6 and 6.6, CH=) and 6.94 (2 H, s, ArH).

(2*S*,3*R*)-2-(2-Methylpropyl)-*N*-(2,4,6-trimethylphenylsulfonyl)-3-vinylaziridine 35

By use of a procedure identical with that described for the preparation of **30** from **29**, the alcohol **34** (1.04 g, 3.18 mmol) was converted into 0.963 g (3.13 mmol, 98%) of the title compound **35**, as a colourless oil [Found (FAB): $(M + H)^+$, 308.1678. $C_{17}H_{25}NO_2S$ requires *M* + H, 308.1684]; $[\alpha]_D^{25}$ −3.12 (*c* 0.915 in $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 0.85 (3 H, d, *J* 5.3, CMe), 0.87 (3 H, d, *J* 5.3, CMe), 1.30 (1 H, m, C*H*H), 1.38 (1 H, m, CH*H*), 1.56 (1 H, m, CH), 2.30 (3 H, s, CMe), 2.69 (6 H, s, CMe), 2.96 (1 H, ddd, *J* 13.5, 7.3 and 0.5, 2-H), 3.35 (1 H, t, *J* 7.3, 3-H), 5.25 (1 H, m, C*H*H), 5.34 (1 H, m, CH*H*), 5.61 (1 H, ddd, *J* 17.2, 10.2 and 6.9, CH=) and 6.94 (2 H, s, ArH); *m*/*z* (FAB-LRMS) 308 (MH^+), 306, 183 (base peak), 124 and 119.

Benzyl (2*E*,4*R*,5*S*)-7-methyl-4,5-[*N*-(2,4,6-trimethylphenylsulfonyl)epimino]oct-2-enoate 36

By use of a procedure similar to that described for the preparation of **31** from **30**, the vinylaziridine **35** (0.928 mg, 3.02 mmol) was converted into 886 mg (2.01 mmol, 70% yield based on **35**) of the title compound **36** by successive treatments with O_3 in $CHCl_3$–*n*-hexane (1:1) at −78 °C for 30 min, dimethyl sulfide (2.21 mmol), [(benzyloxycarbonyl)methylene]triphenylphosphorane (6.04 mmol) in $CHCl_3$ at 0 °C for 15 h, and $Pd(PPh_3)_4$ (0.167 mmol) in THF at rt for 17 h.

Compound **36**, colourless crystals, mp 81–82 °C (from *n*-hexane) (Found: C, 67.90; H, 7.20; N, 2.88. $C_{25}H_{31}NO_4S$ requires C, 68.00; H, 7.08; N, 3.17%); $[\alpha]_D^{26}$ −2.47 (*c* 2.41 in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 0.83 (3 H, d, *J* 6.7, CMe), 0.86 (3 H, d, *J* 6.8, CMe), 1.32 (2 H, m, 6-H_2), 1.53 (1 H, m, 7-H), 2.30 (3 H, s, CMe), 2.68 (6 H, s, CMe), 3.05 (1 H, m, 5-H), 3.43 (1 H, m, 4-H), 5.17 (2 H, s, CH_2), 6.08 (1 H, dd, *J* 15.6 and 0.9, CH=), 6.72 (1 H, dd, *J* 15.6 and 6.9, CH=), 6.95 (2 H, s, ArH) and 7.32–7.39 (5 H, m, Ph).

(2*S*)-6-(2-Chlorophenylmethoxycarbonylamino)-*N*-methoxy-*N*-methyl-2-(2,4,6-trimethylphenylsulfonylamino)hexanamide 38

To a stirred solution of N^{ε}-(Cl-Z)-protected (*S*)-lysine **37** (3 g, 9.53 mmol) and Et_3N (3.31 cm^3, 23.8 mmol) in H_2O (10 cm^3) at 0 °C was added 2.50 g (11.4 mmol) of Mts-Cl. After being stirred for 15 h, the mixture was made acidic with saturated aq. citric acid and extracted with EtOAc and the extract was washed with water and dried over $MgSO_4$ to give a crude N^{α}- and N^{ε}-protected lysine as a colourless oil. To a stirred solution of the above N^{α}- and N^{ε}-protected lysine in DMF (10 cm^3) at 0 °C were added HOBt (1.61 g, 10.5 mmol), WSCD (1.82 cm^3, 10.5 mmol) and *N*,*O*-dimethylhydroxylamine hydrochloride (1.02 g, 10.5 mmol). After being stirred at rt for 15 h, the solution was concentrated under reduced pressure and extracted with EtOAc. The extract was washed successively with 5% citric acid, water, 5% $NaHCO_3$ and water, and dried over $MgSO_4$. Usual work-up and flash chromatography over silica gel with *n*-hexane–EtOAc (3:1) gave 3.78 g (7.00 mmol, 74%) of the *title compound* **38** as a colourless crystalline mass, mp 111–113 °C [from *n*-hexane–Et_2O (5:1)] (Found: C, 55.64; H, 6.51; N, 7.58. $C_{25}H_{34}ClN_3O_6S$ requires C, 55.66; H, 6.35; N, 7.78%); $[\alpha]_D^{21}$ +14.7 (*c* 1.39 in $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.30 (4 H, m, CH_2), 1.57 (2 H, m, CH_2), 2.27 (3 H, s, CMe), 2.65 (6 H, s, CMe), 2.98 (3 H, s, NMe), 3.13 (2 H, m, CH_2), 3.51 (3 H, s, OMe), 4.16 (1 H, m, 2-H), 4.85 (1 H, m, NH), 5.21 (2 H, s, CH_2), 5.59 (1 H, d, *J* 9.6, NH), 6.92 (2 H, s, ArH) and 7.24–7.45 (4 H, m, ArH); *m*/*z* (FAB-LRMS) 540 (MH^+), 496, 398, 353 (base peak), 309, 252, 208, 183, 127, 125, 119, 91 and 84.

(3*S*,4*S*)-8-(2-Chlorophenylmethoxycarbonylamino)-4-(2,4,6-trimethylphenylsulfonylamino)oct-1-en-3-ol 40 and (3*R*,4*S*)-8-(2-chlorophenylmethoxycarbonylamino)-4-(2,4,6-trimethylphenylsulfonylamino)oct-1-en-3-ol 41

To a stirred solution of the amide **38** (3 g, 5.56 mmol) in dry THF (10 cm^3) under argon at −78 °C with stirring was added *via* syringe 22 cm^3 (22.2 mmol) of a 1.01 mol dm^{-3} solution of DIBAL in toluene, and the stirring was continued for 1.5 h. EtOAc (2 cm^3) and MeOH (2 cm^3) were added successively to the above mixture at −78 °C, and the stirring was continued at −78 °C for 30 min followed by addition with 1 mol dm^{-3} aq. HCl (20 cm^3). After being stirred at 0 °C for 20 min, the mixture was extracted with EtOAc and the extract was washed with water and dried over $MgSO_4$. Usual work-up gave the crude aldehyde **39** (colourless oil). By use of a procedure similar to that described for the preparation of **27** and **28** from **26**, the above crude aldehyde **39** was converted into allyl alcohols **40** and **41** (diastereomixture 2.71 g, 5.31 mmol, 96%) as a colourless oil by treatment with $ZnCl_2$ (22.2 mmol), LiCl (22.2 mmol), and 1.47 mol dm^{-3} vinylmagnesium chloride (22.2 mmol) in THF at 0 °C for 4 h.

Compounds **40** and **41**, colourless oil (diastereomixture), [Found (FAB): $(M + H)^+$, 509.1866. $C_{25}H_{33}ClN_2O_5S$ requires *M* + H, 509.1877]; *m*/*z* (FAB-LRMS) 509 (MH^+), 465, 367, 349 (base peak), 252, 208, 183, 167, 125 and 119.

(2*S*,3*R*)-2-[4-(2-Chlorophenylmethoxycarbonylamino)butyl]-*N*-(2,4,6-trimethylphenylsulfonyl)-3-vinylaziridine 42 and (2*S*,3*S*)-2-[4-(2-chlorophenylmethoxycarbonylamino)butyl]-*N*-(2,4,6-trimethylphenylsulfonyl)-3-vinylaziridine 43

By use of a procedure similar to that described for the preparation of **30** from **29**, the diastereomixtures **40** and **41** (2.34 g, 4.60 mmol) were converted into vinylaziridines **42** and **43** (diastereomixture 1.96 g, 3.98 mmol, 87%) as a colourless oil [Found (FAB): $(M + H)^+$, 491.1775. $C_{25}H_{31}ClN_2O_4S$ requires *M* + H, 491.1772]; *m*/*z* (FAB-LRMS) 491 (MH^+), 349, 308, 252 (base peak), 208, 183, 167, 125, 119 and 91.

Benzyl (2*E*,4*R*,5*S*)-9-(2-chlorophenylmethoxycarbonylamino)-4,5-[(2,4,6-trimethylphenylsulfonyl)epimino]non-2-enoate 44

By use of a procedure similar to that described for the preparation of **36** from **35**, the diastereomixtures **42** and **43** (1.91 g, 3.90 mmol) were converted into the *cis*-(*E*)-enoate **44** [951 mg, 1.52 mmol, 39% (3 steps)] as a colourless oil, [Found (FAB): $(M + H)^+$, 625.2133. $C_{33}H_{37}ClN_2O_6S$ requires *M* + H, 625.2139]; $[\alpha]_D^{24}$ −43.5 (*c* 1.51 in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 1.24 (2 H, m, CH_2), 1.40 (2 H, m, CH_2), 1.50 (2 H, m, CH_2), 2.28 (3 H, s, CMe), 2.67 (6 H, s, CMe), 2.95 (1 H, m, 5-H), 3.06 (2 H, dd, *J* 12.9 and 6.4, CH_2), 3.46 (1 H, m, 4-H), 4.73 (1 H, m, NH), 5.16 (2 H, s, CH_2), 5.20 (2 H, s, CH_2), 6.09 (1 H, dd, *J* 15.6 and 1.0, CH=), 6.71 (1 H, dd, *J* 15.6 and 6.7, CH=), 6.94 (2 H, s, ArH) and 7.21–7.43 (9 H, m, ArH); *m*/*z* (FAB-LRMS) 625 (MH^+), 441, 252 (base peak), 208, 154, 136, 125, 119 and 91.

(1*S*)-1-[(4*S*)-*N*-(*tert*-Butoxycarbonyl)-2,2-dimethyloxazolidin-4-yl]prop-2-en-1-ol 46 and (1*R*)-1-[(4*S*)-*N*-(*tert*-butoxycarbonyl)-2,2-dimethyloxazolidin-4-yl]prop-2-en-1-ol 47

By use of a procedure similar to that described for the preparation of **27** and **28** from **26**, the aldehyde **45** (3.95 g, 17.2 mmol) was converted into allyl alcohols **46** and **47** (diastereomixture 2.91 g, 11.3 mmol, 59%) as a colourless oil by treatment with $ZnCl_2$ (51.6 mmol), LiCl (51.6 mmol), and 1.60 mol dm^{-3} vinylmagnesium chloride (51.6 mmol) in THF at 0 °C for 4 h.

Compounds **46** and **47**, colourless oil (diastereomixture) [Found (FAB): $(M + H)^+$, 258.1710. $C_{13}H_{23}NO_4$ requires $M + H$, 258.1705]; *m*/*z* (FAB-LRMS) 258 (MH^+), 202, 200, 189, 184 (base peak), 144, 131, 100 and 57.

(2*S*,3*S*)-2-(2,4,6-Trimethylphenylsulfonylamino)pent-4-ene-1,3-diol 48 and (2*S*,3*R*)-2-(2,4,6-trimethylphenylsulfonylamino)pent-4-ene-1,3-diol 49

TFA (15 cm^3) and H_2O (2.11 cm^3, 117 mmol) were added to 3.02 g (11.7 mmol) of the allyl alcohols **46** and **47** (diastereomixture) at 0 °C, and the mixture was stirred for 1 h. The mixture was concentrated under reduced pressure to give an oily residue, which was washed with *n*-hexane. To the oil in 10 cm^3 of $CHCl_3$ were added at 0 °C successively 3.99 cm^3 (23.5 mmol) of DIPEA and 4.62 g (21.1 mmol) of Mts-Cl. After being stirred for 15 h, the mixture was made acidic with saturated aq. citric acid and extracted with EtOAc and the extract was washed with water and dried over $MgSO_4$. Purification by flash chromatography over silica gel with *n*–hexane–EtOAc (2:3) gave 1.86 g (6.21 mmol, 53%) of the diastereomixture of **48** and **49** as a colourless oil [Found (FAB): $(M + H)^+$, 300.1263. $C_{14}H_{21}NO_4S$ requires $M + H$, 300.1269]; *m*/*z* (FAB-LRMS) 300 (MH^+), 282, 252 (base peak), 242, 183 and 119.

(3*S*,4*S*)-5-Benzyloxy-3-hydroxy-4-(2,4,6-trimethylphenylsulfonylamino)pent-1-ene 50 and (3*R*,4*S*)-5-benzyloxy-3-hydroxy-4-(2,4,6-trimethylphenylsulfonylamino)pent-1-ene 51

Sodium hydride (198 mg of 60% dispersion in mineral oil, 4.94 mmol) was added to a stirred solution of the diastereomixture of **48** and **49** (672 mg, 2.42 mmol) in 3 cm^3 of THF at −40 °C, and the mixture was stirred for 30 min with warming to 0 °C. To the above mixture at 0 °C was added dropwise benzyl bromide (0.294 cm^3, 2.47 mmol), and the mixture was stirred for 2 h. The reaction was quenched with 5 cm^3 of saturated $NaHCO_3$ at 0 °C. The mixture was extracted with EtOAc and the extract was washed successively with water, 1 mol dm^{-3} HCl, water, 5% $NaHCO_3$ and water, and dried over $MgSO_4$. Concentration under reduced pressure gave a residue, which was purified by flash chromatography over silica gel with *n*-hexane–EtOAc (2:1) to give 483 mg (1.24 mmol, 55%) of the diastereomixture of the alcohols **50** and **51**.

Compounds **50** and **51**, colourless oil (diastereomixture) [Found (FAB): $(M + H)^+$, 390.1747. $C_{21}H_{27}NO_4S$ requires $M + H$, 390.1739]; *m*/*z* (FAB-LRMS) 390 (MH^+), 242 (base peak), 183, 149, 119 and 91.

(2*R*,3*R*)-2-(Benzyloxymethyl)-*N*-(2,4,6-trimethylphenylsulfonyl)-3-vinylaziridine 52 and (2*R*,3*S*)-2-(benzyloxymethyl)-*N*-(2,4,6-trimethylphenylsulfonyl)-3-vinylaziridine 53

By use of a procedure identical with that described for the preparation of **30** from **29**, the mixture of the alcohols **50** and **51** (760 mg, 1.95 mmol) was converted into 640 mg (1.72 mmol, 88%) of the diastereomixture of the vinylaziridines **52** and **53** as a colourless oil [Found (FAB): $(M + H)^+$, 372.1626. $C_{21}H_{25}NO_3S$ requires $M + H$, 372.1634]; *m*/*z* (FAB-LRMS) 372 (MH^+), 302, 264 (base peak), 188, 183, 119 and 91.

(2*E*,4*R*,5*R*)-6-Benzyloxy-*N*-methyl-4,5-[(2,4,6-trimethylphenylsulfonyl)epimino]hex-2-enamide 54

By use of a procedure identical with that described for the preparation of the corresponding aldehyde from **30**, the mixture of the vinylaziridines **52** and **53** (580 mg, 1.56 mmol) was converted into the crude diastereomixture of the corresponding aldehydes. To a stirred solution of LiCl (159 mg, 3.75 mmol) in 2 cm^3 of CH_3CN at 0 °C was added *via* syringe DIPEA (0.652 cm^3, 3.75 mmol) and a CH_3CN solution (5 cm^3) of diethoxphosphoryl-*N*-methylacetamide (791 mg, 3.75 mmol), which was prepared by treatment of ethyl diethyloxyphosphorylacetate with methylamine (5 equiv.) in MeOH, and the mixture was stirred at this temperature for 30 min. To the mixture at 0 °C was added dropwise a solution of the above crude aldehydes in CH_3CN (3 cm^3), and the stirring was continued at rt for 12 h. The mixture was concentrated under reduced pressure to leave a semisolid, which was extracted with EtOAc and the extract was washed successively with water, 1 mol dm^{-3} HCl, water, saturated aq. $NaHCO_3$ and water, and dried over $MgSO_4$. Concentration under reduced pressure gave a residue, which was purified by flash chromatography over silica gel with *n*-hexane–EtOAc (5:1) to give a mixture of the enamide **54** and its diastereoisomer. The diastereomixture was treated with $Pd(PPh_3)_4$ (0.042 mmol, 5 mol%) by use of a procedure identical with that described for the preparation of the *cis*-(*E*)-enoate **31** from the mixture of **31** and **32** to give 232 mg [0.541 mmol, 35% (3 steps)] of the *cis*-(*E*)-enamide **54** as a colourless oil [Found (FAB): $(M + H)^+$, 429.1841. $C_{23}H_{28}N_2O_4S$ requires $M + H$, 429.1848]; $[\alpha]_D^{21}$ −54.4 (*c* 1.06 in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 2.29 (3 H, s, CMe), 2.68 (6 H, s, CMe), 2.86 (3 H, d, *J* 4.9, NMe), 3.22 (1 H, m, 5-H), 3.45 (1 H, dd, *J* 11.1 and 6.5, C*H*H), 3.52 (1 H, m, 4-H), 3.53 (1 H, dd, *J* 11.1 and 5.5, CH*H*), 4.36 (2 H, s, CH_2), 5.52 (1 H, d, *J* 4.7, NH), 6.04 (1 H, dd, *J* 15.2 and 0.9, CH=), 6.57 (1 H, dd, *J* 15.2 and 6.9, CH=), 6.94 (2 H, s, ArH) and 7.10–7.33 (5 H, m, Ph); *m*/*z* (FAB-LRMS) 429 (MH^+), 154 (base peak), 119 and 91.

Methyl (2*E*,4*R*,5*R*)-6-benzyloxy-4,5-[(2,4,6-trimethylphenylsulfonyl)epimino]hex-2-enoate 55

By use of a procedure identical with that described for the preparation of **31** from **30**, the mixture of the vinylaziridines **52** and **53** (1.27 g, 3.42 mmol) was converted into the *cis*-(*E*)-enoate **55** [(526 mg, 1.23 mmol, 36% (3 steps)] as a colourless oil [Found (FAB): $(M + H)^+$, 430.1691. $C_{23}H_{27}NO_5S$ requires $M + H$, 430.1688]; $[\alpha]_D^{24}$ −66.9 (*c* 0.352 in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 2.29 (3 H, s, CMe), 2.68 (6 H, s, CMe), 3.27 (1 H, m, 5-H), 3.49 (2 H, m, CH_2), 3.51 (1 H, m, 4-H), 3.73 (3 H, s, OMe), 4.36 (1 H, d, *J* 12.0, C*H*H), 4.41 (1 H, d, *J* 12.0, CH*H*), 6.08 (1 H, dd, *J* 15.6 and 0.9, CH=), 6.67 (1 H, dd, *J* 15.6 and 6.8, CH=), 6.95 (2 H, s, ArH) and 7.13–7.33 (5 H, m, Ph); *m*/*z* (FAB-LRMS) 430 (MH^+), 400, 246, 217, 183, 167 (base peak), 119 and 91.

Mts-L-Val-ψ[(*E*)-CH=CH]-D-Phe-OMe 56 prepared from 10

To a stirred slurry of CuCN (154 mg, 1.72 mmol) in 3 cm^3 of dry THF under argon at −78 °C was added by syringe 1.37 cm^3 (1.72 mmol) of 1.25 mol dm^{-3} BnMgCl in THF, and the mixture was allowed to warm to 0 °C and was stirred at this temperature for 15 min. $BF_3{\cdot}Et_2O$ (0.211 cm^3, 1.72 mmol) was added to the above mixture at −78 °C and the mixture was stirred for 5 min. A solution in dry THF (1 cm^3) of the crude mesyl compound **11**, which was prepared from the *cis*-(*E*)-enoate **10** (151 mg, 0.430 mmol) by the MSA treatment, was added dropwise to the above reagent at −78 °C with stirring, and the stirring was continued for 30 min followed by quenching with 2 cm^3 of a 1:1 saturated aq. NH_4Cl–28% NH_4OH solution. The mixture was extracted with Et_2O and the extract was washed with water and dried over $MgSO_4$. Concentration

under reduced pressure gave a colourless oil, which was purified by flash chromatography over silica gel with *n*-hexane–EtOAc (3:1) to yield 179 mg (0.404 mmol, 94% yield based on **10**) of **56** as a colourless oil [Found (FAB): $(M - H)^-$, 442.2056. $C_{25}H_{33}NO_4S$ requires $M - H$, 442.2052]; $[\alpha]_D^{27}$ +14.3 (*c* 1.0 in $CHCl_3$); $\Delta\varepsilon$ +2.95 (217 nm, isooctane); δ_H(270 MHz; $CDCl_3$) 0.69 (3 H, d, *J* 7.3, CMe), 0.72 (3 H, d, *J* 7.3, CMe), 1.66 (1 H, m, 6-H), 2.28 (3 H, s, CMe), 2.53 (1 H, dd, *J* 13.5 and 7.6, C*H*H), 2.59 (6 H, s, CMe), 2.90 (1 H, dd, *J* 13.5 and 7.6, CH*H*), 3.05 (1 H, dd, *J* 15.2 and 7.6, 2-H), 3.48 (1 H, m, 5-H), 3.60 (3 H, s, OMe), 4.49 (1 H, d, *J* 7.6, NH), 5.06 (1 H, ddd, *J* 15.5, 7.6 and 1.5, CH=), 5.35 (1 H, ddd, *J* 15.5, 8.3 and 1.1, CH=), 6.91 (2 H, s, ArH) and 7.01–7.38 (5 H, m, Ph); *m*/*z* (FAB-LRMS) 442 [$(M - H)^-$], 308 (base peak), 198, 183, 153 and 151.

Mts-L-Val-ψ[(*E*)-CH=CH]-L-Phe-OMe 57 prepared from 10

To a stirred solution of CuCN (358 mg, 4 mmol) and LiCl (339 mg, 8 mmol) in dry THF (8 cm^3) under argon at −78 °C was added *via* syringe 7.27 cm^3 (4 mmol) of 0.55 mol dm^{-3} BnMgCl in THF, and the mixture was allowed to warm to 0 °C and was stirred at this temperature for 15 min. A solution of the *cis*-(*E*)-enoate **10** (351 mg, 1 mmol) in dry THF (2 cm^3) was added dropwise to the above reagent at −78 °C with stirring, and the stirring was continued for 30 min followed by quenching with 5 cm^3 of a 1:1 saturated aq. NH_4Cl–28% NH_4OH solution. The mixture was extracted with Et_2O and the extract was washed with water and dried over $MgSO_4$. Concentration under reduced pressure gave an oily residue, which was purified by flash chromatography over silica gel with *n*-hexane–EtOAc (3:1) to yield 333 mg (0.75 mmol, 75%) of **57** as colourless crystals, mp 85–87 °C (from Et_2O) (Found: C, 67.65; H, 7.53; N, 3.08. $C_{25}H_{33}NO_4S$ requires C, 67.69; H, 7.50; N, 3.16%); $[\alpha]_D^{26}$ −69.2 (*c* 0.697 in $CHCl_3$); $\Delta\varepsilon$ −11.09 (219 nm, isooctane); δ_H(270 MHz; $CDCl_3$) 0.74 (3 H, d, *J* 6.6, CMe), 0.79 (3 H, d, *J* 6.9, CMe), 1.69 (1 H, m, 6-H), 2.27 (3 H, s, CMe), 2.52 (1 H, dd, *J* 13.5 and 6.3, C*H*H), 2.62 (6 H, s, CMe), 2.87 (1 H, dd, *J* 13.5 and 8.6, CH*H*), 3.07 (1 H, m, 2-H), 3.51 (1 H, m, 5-H), 3.55 (3 H, s, OMe), 4.43 (1 H, d, *J* 7.9, NH), 5.19 (1 H, ddd, *J* 15.5, 7.3 and 1.0, CH=), 5.36 (1 H, ddd, *J* 15.5, 7.6 and 1.0, CH=), 6.93 (2 H, s, ArH) and 7.04–7.29 (5 H, m, Ph); *m*/*z* (FAB-LRMS) 442 [$(M - H)^-$], 308 (base peak), 198, 183 and 153.

Mts-L-Val-ψ[(*E*)-CH=CH]-L-Phe-OMe 57 prepared from 14

By use of a procedure similar to that described for the preparation of **56** from **11**, the crude mesyl derivative **15**, which was prepared from the *trans*-(*E*)-enoate **14** (120 mg, 0.342 mmol) by MSA treatment, was converted into Mts-L-Val-ψ[(*E*)-CH=CH]-L-Phe-OMe **57** (135 mg, 0.305 mmol, 89% yield based on **14**) by treatment with BnCu(CN)MgCl·BF_3 (1.37 mmol) in THF at −78 °C for 30 min.

Compound **57**, colourless crystals, mp 82 °C [from *n*-hexane–Et_2O (5:1)] (Found: C, 67.77; H, 7.73; N, 3.07. $C_{25}H_{33}NO_4S$ requires C, 67.69; H, 7.50; N, 3.16%); $[\alpha]_D^{19}$ −64.8 (*c* 0.603 in $CHCl_3$); $\Delta\varepsilon$ −7.16 (221 nm, isooctane); δ_H(270 MHz; $CDCl_3$) 0.73 (3 H, d, *J* 6.9, CMe), 0.79 (3 H, d, *J* 6.9, CMe), 1.69 (1 H, m, 6-H), 2.27 (3 H, s, CMe), 2.52 (1 H, dd, *J* 13.5 and 6.3, C*H*H), 2.62 (6 H, s, CMe), 2.86 (1 H, dd, *J* 13.5 and 8.6, CH*H*), 3.07 (1 H, m, 2-H), 3.51 (1 H, m, 5-H), 3.55 (3 H, s, OMe), 4.45 (1 H, d, *J* 7.9, NH), 5.19 (1 H, ddd, *J* 15.5, 7.6 and 1.0, CH=), 5.35 (1 H, ddd, *J* 15.5, 7.9 and 1.0, CH=), 6.93 (2 H, s, ArH) and 7.04–7.29 (5 H, m, Ph).

Mts-L-Val-ψ[(*E*)-CH=CH]-D-Phe-OMe 56 prepared from 14

By use of a procedure similar to that described for the preparation of **57** from **10**, the *trans*-(*E*)-enoate **14** (56.2 mg, 0.160 mmol) was converted into Mts-L-Val-ψ[(*E*)-CH=CH]-D-Phe-OMe **56** (54.4 mg, 0.123 mmol, 77%) as a colourless oil by treatment with BnCu(CN)MgCl·2LiCl (0.640 mmol) in THF at −78 °C for 30 min.

Compound **56**, colourless oil [Found (FAB): $(M - H)^-$, 442.2050. $C_{25}H_{33}NO_4S$ requires $M - H$, 442.2052]; $[\alpha]_D^{24}$ +16.8 (*c* 2.22 in $CHCl_3$); $\Delta\varepsilon$ +4.21 (214 nm, isooctane); δ_H(270 MHz; $CDCl_3$) 0.69 (3 H, d, *J* 7.3, CMe), 0.72 (3 H, d, *J* 7.3, CMe), 1.64 (1 H, m, 6-H), 2.28 (3 H, s, CMe), 2.53 (1 H, dd, *J* 13.5 and 7.6, C*H*H), 2.59 (6 H, s, CMe), 2.90 (1 H, dd, *J* 13.5 and 7.6, CH*H*), 3.05 (1 H, dd, *J* 15.2 and 7.6, 2-H), 3.47 (1 H, m, 5-H), 3.60 (3 H, s, OMe), 4.51 (1 H, d, *J* 6.9, NH), 5.06 (1 H, ddd, *J* 15.5, 7.6 and 0.5, CH=), 5.35 (1 H, ddd, *J* 15.5, 8.3 and 0.8, CH=), 6.91 (2 H, s, ArH) and 7.01–7.38 (5 H, m, Ph); *m*/*z* (FAB-LRMS) 442 [$(M - H)^-$], 308, 198, 183, 153 and 151 (base peak).

Methyl (2*E*,4*R*,5*R*)-4-(methylsulfonyloxy)-6-phenyl-5-(2,4,6-trimethylphenylsulfonylamino)hex-2-enoate 58

By use of a procedure similar to that described for the preparation of **11** from **10**, the *cis*-(*E*)-enoate **31** (42.3 mg, 0.106 mmol) was converted into the γ-mesyloxy-α,β-enoate **58** by treatment with MSA in $CHCl_3$.

Compound **58**, colourless oil (crude), δ_H(300 MHz; $CDCl_3$) 2.27 (3 H, s, CMe), 2.43 (6 H, s, CMe), 2.54 (1 H, dd, *J* 14.1 and 8.8, C*H*H), 3.03 (1 H, dd, *J* 14.1 and 6.2, CH*H*), 3.07 (3 H, s, SMe), 3.69 (1 H, m, 5-H), 3.76 (3 H, s, OMe), 4.88 (1 H, d, *J* 7.3, NH), 5.47 (1 H, m, 4-H), 6.09 (1 H, dd, *J* 15.8 and 1.5, CH=), 6.80 (2 H, s, Ph), 6.91 (1 H, dd, *J* 15.8 and 5.8, CH=) and 6.94–7.18 (5 H, m, Ph); *m*/*z* (FAB-LRMS) 496 (MH^+), 400, 302,183, 149 (base peak), 119 and 91.

Mts-D-Phe-ψ[(*E*)-CH=CH]-L-Leu-OMe 59

By use of a procedure similar to that described for the preparation of **56** from **11**, the crude mesyl derivative **58**, which was prepared from the *cis*-(*E*)-enoate **31** (42.3 mg, 0.106 mmol), was converted into Mts-D-Phe-ψ[(*E*)-CH=CH]-L-Leu-OMe **59** (41.7 mg, 0.091 mmol, 86% yield based on **31**) by treatment with $Bu^iCu(CN)MgCl{\cdot}BF_3$ (0.424 mmol) in THF at −78 °C for 30 min.

Compound **59**, colourless crystals, mp 74–75 °C [from *n*-hexane–Et_2O (5:1)] (Found: C, 67.95; H, 7.63; N, 2.86. $C_{26}H_{35}NO_4S$ requires C, 68.24; H, 7.71; N, 3.06%); $[\alpha]_D^{18}$ −11.2 (*c* 0.624 in $CHCl_3$); $\Delta\varepsilon$ −5.97 (221 nm, isooctane); δ_H[270 MHz; $CDCl_3$ containing tris-{3-[heptafluoropropyl(hydroxy)methylene]-*d*-camphorato}europium(III)] 0.77 (3 H, d, *J* 6.6, CMe), 0.81 (3 H, d, *J* 6.3, CMe), 1.18 (1 H, m, C*H*H), 1.29 (1 H, m, CH*H*), 1.48 (1 H, m, CH), 2.29 (3 H, s, CMe), 2.54 (6 H, s, CMe), 2.77 (1 H, dd, *J* 13.5 and 7.3, C*H*H), 2.85 (1 H, dd, *J* 13.5 and 6.3, CH*H*), 2.99 (1 H, dd, *J* 15.2 and 7.6, 2-H), 3.72 (3 H, s, OMe), 3.98 (1 H, m, 5-H), 4.56 (1 H, d, *J* 6.3, NH), 5.36 (1 H, dd, *J* 15.7 and 5.9, CH=), 5.42 (1 H, dd, *J* 15.7 and 7.8, CH=), 6.90 (2 H, s, ArH) and 7.02–7.27 (5 H, m, Ph); *m*/*z* (FAB-LRMS) 480 (MNa^+), 458 (MH^+), 456 (MH^-), 398 (base peak), 366, 259, 227, 199, 183, 129, 119 and 91.

Mts-D-Phe-ψ[(*E*)-CH=CH]-D-Leu-OMe 60

By use of a procedure similar to that described for the preparation of **57** from **10**, the *cis*-(*E*)-enoate **31** (53.3 mg, 0.133 mmol) was converted into Mts-D-Phe-ψ[(*E*)-CH=CH]-D-Leu-OMe **60** (56.0 mg, 0.122 mmol, 92%) by treatment with $Bu^iCu(CN)MgCl{\cdot}2LiCl$ (0.534 mmol) in THF at −78 °C for 30 min.

Compound **60**, colourless crystals, mp 109–110 °C [from *n*-hexane–Et_2O (5:1)] (Found: C, 67.97; H, 7.70; N, 3.06. $C_{26}H_{35}NO_4S$ requires C, 68.24; H, 7.71; N, 3.06%); $[\alpha]_D^{18}$ +56.0 (*c* 0.603 in $CHCl_3$); $\Delta\varepsilon$ +5.64 (216 nm, isooctane); δ_H(270 MHz; $CDCl_3$) 0.81 (3 H, d, *J* 6.3, CMe), 0.83 (3 H, d, *J* 6.3, CMe), 1.14 (1 H, m, C*H*H), 1.36 (1 H, m, CH*H*), 1.46 (1 H, m, CH), 2.28 (3 H, s, CMe), 2.50 (6 H, s, CMe), 2.80 (2 H, d, *J* 6.6, 6-H_2),

2.89 (1 H, dd, *J* 15.2 and 7.6, 2-H), 3.60 (3 H, s, OMe), 3.90 (1 H, m, 5-H), 4.46 (1 H, d, *J* 6.6, NH), 5.27 (1 H, dd, *J* 15.5 and 7.6, CH=), 5.35 (1 H, dd, *J* 15.2 and 6.6, CH=), 6.88 (2 H, s, ArH) and 7.00–7.27 (5 H, m, Ph); *m*/*z* (FAB-LRMS) 480 (MNa^+), 458 (MH^+), 456 (MH^-), 398 (base peak), 366, 259, 227, 199, 183, 129, 119 and 91.

Benzyl (2*E*,4*S*,5*S*)-7-methyl-4-(methylsulfonyloxy)-5-(2,4,6-trimethylphenylsulfonylamino)oct-2-enoate 61

By use of a procedure similar to that described for the preparation of **11** from **10**, the *cis*-(*E*)-enoate **36** (94.9 mg, 0.215 mmol) was converted into the γ-mesyloxy-α,β-enoate **61** by treatment with MSA in $CHCl_3$.

Compound **61**, colourless oil (crude), δ_H(270 MHz; $CDCl_3$) 0.64 (3 H, d, *J* 5.9, CMe), 0.82 (3 H, d, *J* 5.9, CMe), 1.24 (2 H, m, 6-H_2), 1.43 (1 H, m, 7-H), 2.28 (3 H, s, CMe), 2.62 (6 H, s, CMe), 3.01 (3 H, s, SMe), 3.59 (1 H, m, 5-H), 4.56 (1 H, d, *J* 8.6, NH), 5.18 (2 H, s, CH_2), 5.24 (1 H, m, 4-H), 6.05 (1 H, dd, *J* 15.8 and 1.7, CH=), 6.82 (1 H, dd, *J* 15.8 and 5.9, CH=), 6.93 (2 H, s, ArH) and 7.39 (5 H, m, Ph); *m*/*z* (FAB-LRMS) 538 (MH^+), 536 (MH^-), 442, 352 (base peak), 268, 183, 152, 119 and 91.

Mts-L-Leu-ψ[(*E*)-CH=CH]-D-Phe-OBn 62

By use of a procedure similar to that described for the preparation of **56** from **11**, the crude mesyl derivative **61**, which was prepared from the *cis*-(*E*)-enoate **36** (94.9 mg, 0.215 mmol), was converted into Mts-L-Leu-ψ[(*E*)-CH=CH]-D-Phe-OBn **62** (103 mg, 0.192 mmol, 89% yield based on **36**) by treatment with BnCu(CN)MgCl·BF_3 (0.860 mmol) in THF at −78 °C for 30 min.

Compound **62**, colourless crystals, mp 81 °C [from *n*-hexane–Et_2O (3:1)] (Found: C, 71.97; H, 7.43; N, 2.38. $C_{32}H_{39}NO_4S$ requires C, 72.01; H, 7.36; N, 2.62%); $[\alpha]_D^{28}$ 0 (*c* 2.682 in $CHCl_3$); Δε +2.74 (210 nm, isooctane); δ_H(270 MHz; $CDCl_3$) 0.74 (3 H, d, *J* 6.3, CMe), 0.76 (3 H, d, *J* 6.3, CMe), 1.20 (2 H, m, 6-H_2), 1.35 (1 H, m, 7-H), 2.25 (3 H, s, CMe), 2.52 (1 H, dd, *J* 13.5 and 7.3, C*H*H), 2.57 (6 H, s, CMe), 2.88 (1 H, dd, *J* 13.5 and 8.3, CH*H*), 3.10 (1 H, dd, *J* 15.5 and 7.6, 2-H), 3.68 (1 H, m, 5-H), 4.29 (1 H, m, NH), 5.03 (2 H, s, CH_2), 5.05 (1 H, dd, *J* 15.5 and 7.3, CH=), 5.42 (1 H, dd, *J* 15.5 and 8.2, CH=), 6.89 (2 H, s, ArH) and 6.99–7.35 (10 H, m, Ph).

Mts-L-Leu-ψ[(*E*)-CH=CH]-L-Phe-OBn 63

By use of a procedure similar to that described for the preparation of **57** from **10**, the *cis*-(*E*)-enoate **36** (71.3 mg, 0.161 mmol) was converted into Mts-L-Leu-ψ[(*E*)-CH=CH]-L-Phe-OBn **63** (78.6 mg, 0.147 mmol, 91%) by treatment with BnCu(CN)MgCl·2LiCl (0.646 mmol) in THF at −78 °C for 30 min.

Compound **63**, colourless crystals, mp 102–104 °C [from EtOAc–Et_2O (1:5)] (Found: C, 71.71; H, 7.32; N, 2.41. $C_{32}H_{39}NO_4S$ requires C, 72.01; H, 7.36; N, 2.62%); $[\alpha]_D^{29}$ −0.392 (*c* 2.04 in $CHCl_3$); Δε −1.11 (214 nm, isooctane); δ_H(300 MHz; $CDCl_3$) 0.76 (3 H, d, *J* 1.8, CMe), 0.78 (3 H, d, *J* 1.8, CMe), 1.24 (2 H, m, 6-H_2), 1.47 (1 H, m, 7-H), 2.99 (3 H, s, CMe), 2.53 (1 H, dd, *J* 13.6 and 6.1, C*H*H), 2.60 (6 H, s, CMe), 2.87 (1 H, dd, *J* 13.6 and 9.1, CH*H*), 3.09 (1 H, m, 2-H), 3.71 (1 H, m, 5-H), 4.28 (1 H, d, *J* 7.5, NH), 4.98 (2 H, s, CH_2), 5.15 (1 H, ddd, *J* 15.5, 7.6 and 0.7, CH=), 5.41 (1 H, ddd, *J* 15.5, 8.2 and 0.7, CH=), 6.91 (2 H, s, ArH) and 7.01–7.33 (10 H, m, Ph).

Benzyl (2*E*,4*S*,5*S*)-9-[(2-chlorophenyl)methoxycarbonylamino]-4-(methylsulfonyloxy)-5-(2,4,6-trimethylphenylsulfonylamino)-non-2-enoate 64

By use of a procedure similar to that described for the preparation of **11** from **10**, the *cis*-(*E*)-enoate **44** (678 mg, 1.08 mmol) was converted into the γ-mesyloxy-α,β-enoate **64** by treatment with MSA in $CHCl_3$.

Compound **64**, colourless oil (crude), δ_H(300 MHz; $CDCl_3$) 1.09 (2 H, m, CH_2), 1.32 (2 H, m, CH_2), 1.44 (1 H, m, C*H*H), 1.60 (1 H, m, CH*H*), 2.25 (3 H, s, CMe), 2.60 (6 H, s, CMe), 3.00 (3 H, s, SMe), 3.04 (2 H, m, CH_2), 3.51 (1 H, m, 5-H), 4.88 (1 H, t, *J* 5.9, NH), 5.15 (2 H, s, CH_2), 5.17 (1 H, m, 4-H), 5.20 (2 H, s, CH_2), 5.56 (1 H, d, *J* 8.2, NH), 6.02 (1 H, dd, *J* 15.7 and 1.4, CH=), 6.83 (1 H, dd, *J* 15.7 and 5.5, CH=), 6.90 (2 H, s, ArH) and 7.24–7.44 (9 H, m, ArH); *m*/*z* (FAB-LRMS) 721 (MH^+), 625 (base peak), 307, 289, 252, 208, 119 and 91.

Mts-L-Lys(Cl-Z)-ψ[(*E*)-CH=CH]-D-Ala-OBn 65

To a stirred slurry of CuCN (390 mg, 4.34 mmol) in 12 cm^3 of dry THF under argon at −78 °C was added by syringe 2.89 cm^3 (4.34 mmol) of 1.5 mol dm^{-3} MeLi·LiBr in Et_2O, and the mixture was allowed to warm to 0 °C and was stirred at this temperature for 15 min. BF_3·Et_2O (0.533 cm^3, 4.34 mmol) was added to the above mixture at −78 °C and the mixture was stirred for 5 min. A solution in dry THF (3 cm^3) of the crude mesyl compound **64**, which was prepared from the *cis*-(*E*)-enoate **44** (678 mg, 1.08 mmol), was added dropwise to the above reagent at −78 °C with stirring, and the stirring was continued for 30 min followed by quenching with 6 cm^3 of a 1:1 saturated aq. NH_4Cl–28% NH_4OH solution. The mixture was extracted with Et_2O and the extract was washed with water and dried over $MgSO_4$. Concentration under reduced pressure gave a colourless oil, which was purified by flash chromatography over silica gel with *n*-hexane–EtOAc (3:1) to yield 502 mg (0.782 mmol, 72% yield based on **44**) of compound **65** as a colourless oil, [Found (FAB): $(M - H)^-$, 639.2300. $C_{34}H_{41}ClN_2O_6S$ requires *M* − H, 639.2295]; $[\alpha]_D^{19}$ −5.64 (*c* 2.20 in $CHCl_3$); Δε +2.83 (223 nm, isooctane); δ_H(270 MHz; $CDCl_3$) 1.01 (3 H, d, *J* 5.3, CMe), 1.26 (2 H, m, CH_2), 1.41 (4 H, m, CH_2), 2.25 (3 H, s, CMe), 2.58 (6 H, s, CMe), 2.89 (1 H, m, 2-H), 3.11 (2 H, m, CH_2), 3.69 (1 H, m, 5-H), 4.78 (1 H, d, *J* 7.3, NH), 4.88 (1 H, m, NH), 5.07 (2 H, s, CH_2), 5.12 (1 H, ddd, *J* 15.5, 7.3 and 1.5, CH=), 5.21 (2 H, s, CH_2), 5.45 (1 H, dd, *J* 15.5 and 6.9, CH=), 6.88 (2 H, s, ArH) and 7.22–7.44 (9 H, m, ArH); *m*/*z* (FAB-LRMS) 639 [$(M - H)^-$], 497, 471, 305, 198, 183, 168, 153, 151 and 122 (base peak).

Mts-L-Lys(Cl-Z)-ψ[(*E*)-CH=CH]-L-Ala-OBn 66

To a stirred solution of CuCN (32.3 mg, 0.359 mmol) and LiCl (30.4 mg, 0.718 mmol) in dry THF (1 cm^3) under argon at −78 °C was added *via* syringe 0.240 cm^3 (0.359 mmol) of 1.5 mol dm^{-3} MeLi·LiBr in THF, and the mixture was allowed to warm to 0 °C and was stirred at this temperature for 15 min. A solution of the *cis*-(*E*)-enoate **44** (56.1 mg, 0.0897 mmol) in dry THF (1 cm^3) was added dropwise to the above reagent at −78 °C with stirring, and the stirring was continued for 30 min followed by quenching with 1 cm^3 of a 1:1 saturated aq. NH_4Cl–28% NH_4OH solution. The mixture was extracted with Et_2O and the extract was washed with water and dried over $MgSO_4$. Concentration under reduced pressure gave an oily residue, which was purified by flash chromatography over silica gel with *n*-hexane–EtOAc (3:1) to yield 55.8 mg (0.0870 mmol, 97%) of compound **66** as a colourless oil, [Found (FAB): $(M - H)^-$, 639.2292. $C_{34}H_{41}ClN_2O_6S$ requires *M* − H, 639.2296]; $[\alpha]_D^{21}$ −14.1 (*c* 1.34 in $CHCl_3$); Δε −6.00 (216 nm, isooctane); δ_H(270 MHz; $CDCl_3$) 1.01 (3 H, d, *J* 6.9, CMe), 1.26 (2 H, m, CH_2), 1.41 (4 H, m, CH_2), 2.25 (3 H, s, CMe), 2.59 (6 H, s, CMe), 2.89 (1 H, m, 2-H), 3.11 (2 H, m, CH_2), 3.66 (1 H, m, 5-H), 4.67 (1 H, d, *J* 7.3, NH), 4.82 (1 H, m, NH), 5.05 (2 H, s, CH_2), 5.13 (1 H, dd, *J* 15.5 and 7.6, CH=), 5.22 (2 H, s, CH_2), 5.36 (1 H, dd, *J* 15.5 and 7.6, CH=), 6.89 (2 H, s, ArH) and 7.23–7.45 (9 H, m, ArH); *m*/*z* (FAB-LRMS) 639 [$(M - H)^-$], 497, 471, 310, 305 (base peak), 198, 183, 168, 153 and 122.

6-Benzyloxy-(2*E*,4*S*,5*S*)-*N*-methyl-4-(methylsulfonyloxy)-5-(2,4,6-trimethylphenylsulfonylamino)hex-2-enamide 67

By use of a procedure similar to that described for the preparation of **11** from **10**, the *cis*-(*E*)-enamide **54** (85 mg, 0.198 mmol) was converted into the crude γ-mesyloxy-α,β-enamide **67** (colourless oil) by treatment with MSA in $CHCl_3$.

Compound **67**, colourless oil (crude), δ_H(300 MHz; $CDCl_3$) 2.29 (3 H, s, CMe), 2.58 (6 H, s, CMe), 2.85 (3 H, d, *J* 4.9, NMe), 3.00 (3 H, s, SMe), 3.26 (1 H, dd, *J* 9.7 and 5.2, C*H*H), 3.46 (1 H, dd, *J* 9.7 and 4.0, CH*H*), 3.52 (1 H, m, 5-H), 4.20 (1 H, m, 4-H), 4.35 (2 H, s, CH_2), 5.32 (1 H, d, *J* 8.9, NH), 5.76 (1 H, m, CONH), 6.07 (1 H, dd, *J* 15.4 and 1.2, CH=), 6.62 (1 H, dd, *J* 15.4 and 6.5, CH=), 6.91 (2 H, s, ArH) and 7.19–7.36 (5 H, m, Ph); *m*/*z* (FAB-LRMS) 525 (MH^+), 475 (base peak), 429, 391, 279, 167, 149, 119 and 91.

Mts-L-Ser(*O*-Bn)-ψ[(*E*)-CH=CH]-D-Ala-NHMe 68

By use of a procedure identical with that described for the preparation of **65** from **64**, the above crude mesyl compound **67**, which was prepared from the *cis*-(*E*)-enamide **54** (85 mg, 0.198 mmol), was converted into Mts-L-Ser(*O*-Bn)-ψ[(*E*)-CH=CH]-D-Ala-NHMe **68** (79 mg, 0.178 mmol, 90% based on **54**) by treatment with MeCu(CN)Li·LiBr·BF_3 (0.792 mmol) in THF at −78 °C for 30 min.

Compound **68**, colourless oil [Found (FAB): $(M + H)^+$, 445.2156. $C_{24}H_{32}N_2O_4S$ requires *M* + H, 445.2161]; $[\alpha]_D^{21}$ −29.7 (*c* 1.04 in $CHCl_3$); Δε +0.945 (221 nm, isooctane); δ_H(300 MHz; $CDCl_3$) 1.18 (3 H, d, *J* 7.1, CMe), 2.32 (3 H, s, CMe), 2.57 (6 H, s, CMe), 2.74 (3 H, d, *J* 4.7, NMe), 2.89 (1 H, m, 2-H), 3.39 (2 H, d, *J* 5.9, CH_2), 3.69 (1 H, m, 5-H), 4.41 (2 H, s, CH_2), 5.20 (1 H, d, *J* 4.2, NH), 5.50 (1 H, dd, *J* 15.5 and 7.0, CH=), 5.58 (1 H, dd, *J* 15.5 and 7.6, CH=), 6.35 (1 H, m, CONH), 6.93 (2 H, s, ArH) and 7.19–7.36 (5 H, m, Ph); *m*/*z* (FAB-LRMS) 445 (MH^+), 246, 167 (base peak), 149, 119 and 91.

Mts-L-Ser(*O*-Bn)-ψ[(*E*)-CH=CH]-L-Ala-NHMe 69

By use of a procedure identical with that described for the preparation of **66** from **44**, the *cis*-(*E*)-enamide **54** (39 mg, 0.091 mmol) was converted into Mts-L-Ser(*O*-Bn)-ψ[(*E*)-CH=CH]-L-Ala-NHMe **69** (35 mg, 0.079 mmol, 87%) by treatment with MeCu(CN)Li·LiBr·BF_3 (0.364 mmol) in THF at −78 °C for 30 min.

Compound **69**, colourless oil [Found (FAB): $(M + H)^+$, 445.2165. $C_{24}H_{32}N_2O_4S$ requires *M* + H, 445.2161]; $[\alpha]_D^{21}$ −35.1 (*c* 2.71 in $CHCl_3$); Δε −6.96 (208 nm, isooctane); δ_H(300 MHz; $CDCl_3$) 1.21 (3 H, d, *J* 7.1, CMe), 2.30 (3 H, s, CMe), 2.57 (6 H, s, CMe), 2.71 (3 H, d, *J* 4.8, NMe), 2.88 (1 H, m, 2-H), 3.37 (1 H, d, *J* 1.3, C*H*H), 3.39 (1 H, s, CH*H*), 3.72 (1 H, m, 5-H), 4.40 (2 H, s, CH_2), 5.24 (1 H, d, *J* 4.7, NH), 5.47 (1 H, ddd, *J* 15.6, 7.2 and 1.0, CH=), 5.75 (1 H, ddd, *J* 15.6, 7.5 and 0.9, CH=), 6.20 (1 H, m, CONH), 6.93 (2 H, s, ArH) and 7.18–7.38 (5 H, m, Ph); *m*/*z* (FAB-LRMS) 445 (MH^+), 246, 167 (base peak), 156, 149, 119 and 91.

Methyl (2*E*,4*S*,5*S*)-6-benzyloxy-4-trifluoroacetoxy-5-(2,4,6-trimethylphenylsulfonylamino)hex-2-enoate 70

By use of a procedure identical with that described for the preparation of **12** from **10**, the *cis*-(*E*)-enoate **55** (143 mg, 0.332 mmol) was converted into the crude trifluoroacetate **70** as a colourless oil, (crude), δ_H(270 MHz; $CDCl_3$) 2.30 (3 H, s, CMe), 2.57 (6 H, s, CMe), 3.34 (1 H, m, 5-H), 3.73 (3 H, s, OMe), 3.79 (2 H, m, CH_2), 4.38 (2 H, s, CH_2), 5.32 (1 H, m, NH), 5.75 (1 H, m, 4-H), 5.96 (1 H, dd, *J* 15.8 and 0.9, CH=), 6.65 (1 H, dd, *J* 15.8 and 5.9, CH=), 6.91 (2 H, s, ArH) and 7.03–7.41 (5 H, m, Ph); *m*/*z* (FAB-LRMS) 566 (MNa^+), 544 (MH^+), 470, 452, 448, 430, 398, 332, 242 (base peak), 183, 157, 129, 119 and 91.

Methyl (2*E*,4*S*,5*S*)-6-benzyloxy-4-hydroxy-5-(2,4,6-trimethylphenylsulfonylamino)hex-2-enoate 71

Purification of the above crude trifluoroacetate **70** by flash chromatography over silica gel with *n*-hexane–EtOAc (4:1) afforded the hydrolysate **71** (106 mg, 0.236 mmol, 71% yield based on **55**) as a colourless oil, [Found (FAB): $(M + H)^+$, 446.1653. $C_{23}H_{29}NO_6S$ requires *M* + H, 446.1638]; $[\alpha]_D^{28}$ −36.4 (*c* 0.0714 in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 2.31 (3 H, s, CMe), 2.53 (6 H, s, CMe), 3.55 (1 H, m, 5-H), 3.74 (3 H, s, OMe), 3.80 (2 H, m, CH_2), 3.97 (1 H, d, *J* 8.8, 4-H), 4.56 (1 H, d, *J* 10.2, NH), 4.58 (1 H, d, *J* 13.8, C*H*H), 4.68 (1 H, d, *J* 13.8, CH*H*), 5.84 (1 H, dd, *J* 15.8 and 0.6, CH=), 6.95 (2 H, s, ArH), 7.12 (1 H, dd, *J* 15.8 and 8.7, CH=) and 7.01–7.29 (5 H, m, Ph); *m*/*z* (FAB-LRMS) 446 (MH^-), 428, 306, 239 (base peak), 199, 183, 168, 153 and 122.

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