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Amino Acid Synthesis *via* Ring Opening of N-Sulphonyl Aziridine-2-Carboxylate Esters with Organometallic Reagents.

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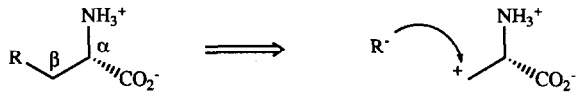
Abstract: Nucleophilic ring opening of optically active N-sulphonyl aziridine-2-carboxylate esters with organometallic reagents has been investigated as a method of preparation of optically active amino acids.

The development of novel methods for the synthesis of amino acids, preferably in an optically pure state, is an area of current endeavour[1]. The plethora of strategies employed for amino acid preparation to date can be divided into three broad categories: resolutions (either classical or enzymatic), asymmetric syntheses (using either stoichiometric or catalytic amounts of either synthetic or enzymatic auxiliaries) and 'chiral pool' elaborations. The commercial availability of the proteinogenic α-amino acids with high optical purity makes these molecules particularly attractive as precursors for this latter, semi-synthetic approach.

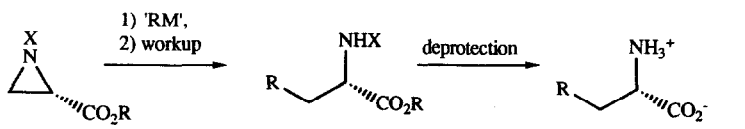
We were interested in developing a versatile synthetic equivalent of the 'β-alanyl cation' chiron suitable for elaboration into β-substituted α-amino acids[2] (Scheme 1):



β-substituted α-amino acid β-alanyl cation

Scheme 1

Studies have already been conducted in this area, most notably by Jacquier[3] and Vederas[4] who have investigated the reactivity of β-halo alanines and serine and threonine β-lactones respectively as synthetic β-alanyl cation equivalents[5]. In addition, Nakajima *et al.*[6] and others[7] have demonstrated that optically pure aziridine-2-carboxylates derived from (S)-serine can behave as synthetic equivalents of the β-alanyl cation upon C-3-N ring opening with heteroatomic nucleophiles (eg. amines[6(ii)7(i-iv)], thiols[6(viii),(ix),7(v-vii)], thio-carboxylic acids[7(viii)], alcohols[6(vi),7(v)], carboxylic acids[6(i),(iii),(vii),7(ix)] and halides[6(iv),7(ix-xi)]). We speculated that this process would be rendered more useful if carbon nucleophiles could be induced to participate in analogous processes (Scheme 2):

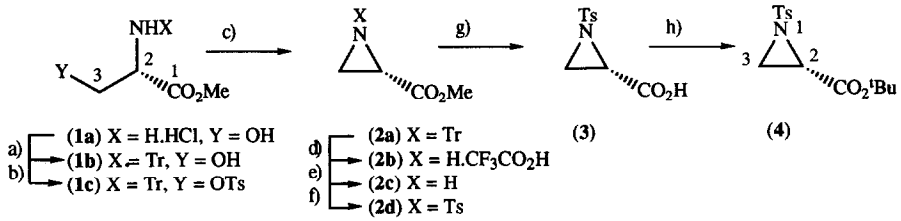


(X = electron withdrawing group) protected β-substituted α-amino acid β-substituted α-amino acid

Scheme 2

Initial realisation of the conjecture was demonstrated by the ring opening of N-tosyl, N-benzyloxycarbonyl, and N-*p*-nitrophenylaziridine-(2S)-methyl esters with stabilised Wittig reagents[8] to provide an entry to the 4-alkylidine-(2S)-glutamic acid family of naturally occurring amino acids. The extension of this process is the subject of this paper[9], which documents an investigation of the reactivity of N-sulphonyl aziridine-(2S)-carboxylate esters towards various organometallic reagents[10] and conversion of the initially obtained adducts to α-amino acids.

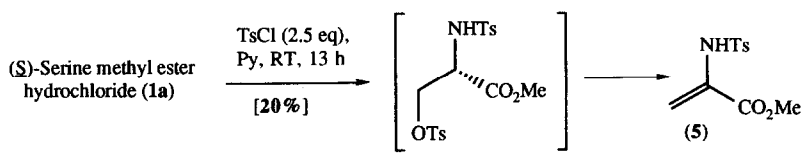
We chose N-tosyl aziridine-(2S)-carboxylic acid tert-butyl ester (**4**) for initial investigation, since it was envisaged that the sulphonyl group would activate the C-N bonds to nucleophilic attack by organometallic reagents. The ^{t}butyl group was anticipated to provide steric inhibition of unwanted reactions at both the ester carbonyl and at the C-2 ring carbon. Synthesis of **4** from (S)-serine methyl ester hydrochloride (**1a**) was achieved in 43% overall yield according to Scheme 3:



a) TrCl (1.0 eq), Et_3N (2 eq), CH_2Cl_2, 0°C, 12 h [**91%**]
b) TsCl (1.1 eq), pyridine, 0°C, 8 h [**94%**]
c) Et_3N (2.0 eq), THF, reflux, 14 h [**72%**]
d) TFA (excess), MeOH (excess), CH_2Cl_2, -10°C, 10 h
e) K_2CO_3 (5.0 eq), CH_2Cl_2, 0°C, 15 min
f) TsCl (2.0 eq), CH_2Cl_2, RT, 2 h [**84%** from (**2a**)]
g) i) LiOH (1.1 eq), 1,4-dioxane, H_2O, 0°C, 15 min, ii) H_3O^+ (excess) [**96%**]
h) $CCl_3C(=NH)O^tBu$ (2.0 eq), $BF_3.Et_2O$ (cat.), cyclohexane, CH_2Cl_2, 0°C, 10 min [**86%**]

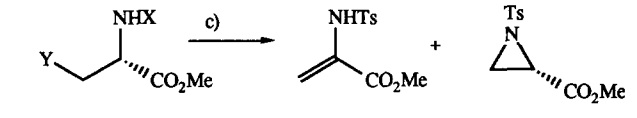
Scheme 3

N-Trityl aziridine-(2S)-carboxylic acid methyl ester (**2a**) was prepared in an analogous fashion to that used by Okawa *et al.*[11] for the preparation of the corresponding benzyl ester. Deprotection of the trityl function using excess trifluoroacetic acid at low temperature in the presence of methanol furnished the unstable trifluoroacetate salt (**2b**), which was basified and reprotected (*in situ*) with tosyl chloride to give the N-sulphonyl protected aziridine-(2S)-carboxylic acid methyl ester (2d). This was saponified and re-esterified with ^{t}butyl trichloroacetimidate[12] to afford the desired ^{t}butyl ester (**4**). Attempted direct synthesis of **2d** by treatment of (S)-serine methyl ester hydrochloride with 2.5 equivalents of tosyl chloride in pyridine resulted in formation of N-tosyl dehydroalanine methyl ester (**5**)[13] (Scheme 4):



Scheme 4

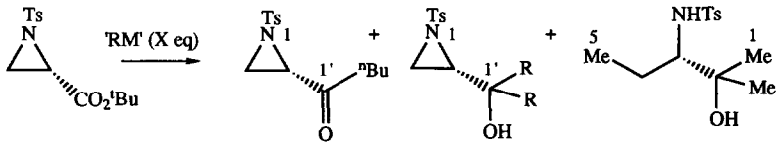
In a related approach N-tosyl-O-mesyl aziridine-(2S)-carboxylic acid methyl ester (**1e**) was exposed to a suspension of potassium carbonate in methanol[14]. On this occasion both aziridinyl (**2d**) and dehydroalanyl (**5**) products resulted, but a ratio of *ca.* 2: 1 in favour of the eliminated product, made the yield (30%) of **2d** unacceptable (Scheme 5):



a) TsCl (1.0 eq), Et_3N (2.0 eq), CH_2Cl_2, 0°C, 12 h [**76%**]
b) MsCl (1.5 eq), Et_3N (1.1 eq), THF, RT, 3 h [**87%**]
c) K_2CO_3 (1.5 eq), MeOH, 0°C, 15 min [**100%**, ratio (**5**): (**2d**) 2: 1]

Scheme 5

Initial attempts at ring opening N-tosyl aziridine-(2S)-carboxylic acid ^{t}butyl ester (**4**) using organolithium and Grignard reagents, not unexpectedly, resulted in preferential attack at the ester carbonyl (Scheme 6, Table 1):

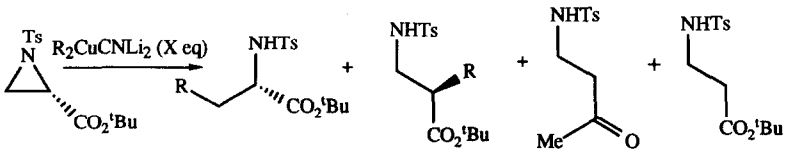


Scheme 6

Entry	R	M	X	Conditions	Products (%) (4)	(6)	(7)	(8)
1	n-Bu	Li	1.8	DME, -78°C, 15 min	31	21	43	-
2	Me	MgCl	3.1	THF i) RT, 1 h, ii) reflux, 30 min	-	-	-	64
3	Me	MgCl	1.1	THF, RT, 5 h	50	-	38	-
4	Me	MgCl	3.1	THF, RT, 19 h	-	-	60	20

Table 1

The use of higher order organocuprates[15] afforded a more promising array of products (Scheme 7, Table 2). Both α-amino acid derivatives (**9**), resulting from ring opening at C-3, and β-amino acid derivatives (**10**), resulting from regioisomeric opening at C-2 were formed. Additionally, reduced products (**11** and **12**) were isolated. These products formally result from hydride delivery to the C-2 ring carbon, a process with precedent in the organocuprate literature[4(ii),15,16].



Scheme 7

Entry	R	X	Solvent	Conditions	Products (%) (4)	(9)	(10)	(11)	(12)
1	Me	(1.2)	THF, ether	-78°C, 10 min	-	20	20	40[a]	-
2	n-Bu	(1.2)	THF	-78°C, 30 min	28	28	15	-	15
3		(1.1)	THF, toluene	-78°C, 10 min	51	25	6	-	12
4		(1.1)	THF, toluene	RT, 22 h	40	30	11	-	11

nb. (a) 7% $TsNH_2$ also isolated.

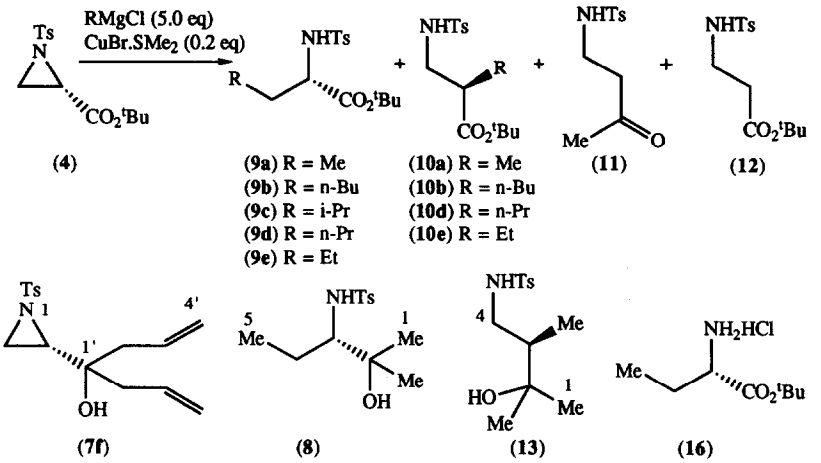
Table 2

We reasoned that the use of Grignard derived, catalytically generated cuprate reagents might reduce these hydride transfer side reactions by virtue of their superior stability and reduced concentration of copper in solution[17]. Accordingly, we investigated the behaviour of various Grignard reagents in the presence of a catalytic quantity of copper(I) bromide-dimethylsulfide[18]. These reactions were experimentally simpler to perform than those employing the corresponding higher order reagents, being considerably less air and moisture sensitive and not requiring pre-formation of the reagent. Additionally, these reactions proved to be 'cleaner', allowing for rapid chromatographic separation of the products after workup (Scheme 8, Table 3).

These reactions were more promising, for although hydride transfer products **11** and **12** were sometimes still observed, conditions could be found under which the major products were those of desired ring opening. The C-3 to C-2 regioselectivity of this ring fission process seemed to reflect a balance between the steric bulk of the nucleophilic organometallic reagent and the intrinsic ambident electrophilicity of the aziridine. Thus, the preference (Table 3, entry 5) for attack by the methyl cuprate at the more hindered C-2 site (over C-3) to give the β-amino acid in a synthetically useful 55% isolated yield, may be attributed to the small size of the methyl nucleophile for which this more electrophilically activated position was accessible. More bulky nucleophiles (Table 3, entries 6-14) demonstrated a preference for attack at the more accessible C-3 carbon affording α-amino acid derivatives as the major products, for example using the *iso*-propyl Grignard reagent (Table 3, entry 12) no opening resulting from attack at C-2 was observed. The anomalous behaviour of the allylic cuprate (Table 3, entry 15), which displayed an affinity for addition to the hindered ester carbonyl, was not unexpected as related results have been found by other workers[20].

Conversion of the protected amino acids to the parent compounds was readily achieved by treatment with 33% HBr in acetic acid[21] followed by ion exchange chromatography (Scheme 9).

The optical integrity of the 'free' amino acids was confirmed by comparison of their optical rotations (where previously reported) with those of the authentic materials in the literature[22]. An additional check on the optical purity of **9e** was made by the independent synthesis of this compound from commercially available **14e** and comparison of its optical rotation with that of the ring opened material (see experimental section).



Scheme 8

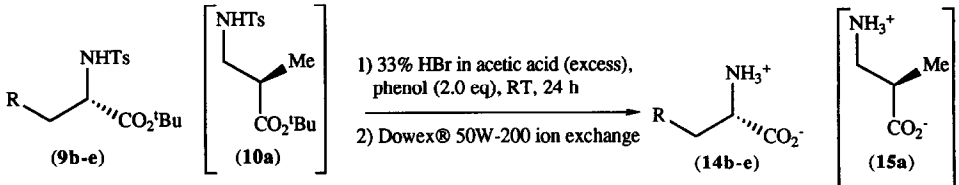
Entry	R	Conditions	Products (%) (4)	(9)	(10)	(11)	(12)	(8)	(13)	(7f)
1	Me	THF, DMS, reflux, 1 h	-	-	-	30	-	40	-	-
2		THF, DMS, -25°C, 3 h	-	-	-	-	-	50	30	-
3		THF, DMS, -25°C, 2 h	-	10	40	-	-	35	-	-
4		THF, DMS, -78°C, 2 h	>95	-	-	-	-	-	-	-
5 (a)		THF, DMS, -20°C, 2 h	-	30	55	-	-	-	-	-
6	n-Bu	THF, DMS, -78°C, 2 h	-	30	30	-	40	-	-	-
7		THF, DMS, -25°C, 2 h	-	50	20	-	20	-	-	-
8		THF, DMS, 0°C, 15 min	-	35	15	-	5	-	-	-
9		THF, HMPA, -12°C, 1 h	-	47	28	-	21	-	-	-
10 (b)		THF, HMPA, -12°C, 1 h	-	45	23	-	28	-	-	-
11	t-Bu	THF, HMPA, -18°C, 2 h	>90	-	-	-	-	-	-	-
12	i-Pr	THF, HMPA, -16°C, 75 min	8	40	-	-	25	-	-	-
13	n-Pr	THF, HMPA, -16°C, 75 min	-	42	21	-	21	-	-	-
14	Et	THF, HMPA, -29°C, 1 h	-	32	20	-	21	-	-	-
15 (c)	Allyl	THF, HMPA, -16°C, 80 min	30	-	-	-	-	-	-	40

nb. (a) 0.8 eq of $CuBr.SMe_2$ and 2.0 eq of Grignard reagent used; (b) COD.CuCl[19] (0.2 eq) used instead of $CuBr.SMe_2$; (c) 10% t-BuNHTs also isolated.

Table 3

The conditions used for liberation of the amino acids from their N-tosyl, tbutyl ester forms (namely 33% HBr in acetic acid in the presence of phenol at ambient temperature for 24 h[21]) were shown not to cause racemisation by the conversion of **9e** (obtained in the above manner) back to **14e** without loss of optical purity and also by allowing prolonged exposure (>1 week) to these conditions, again without detectable loss of optical activity.

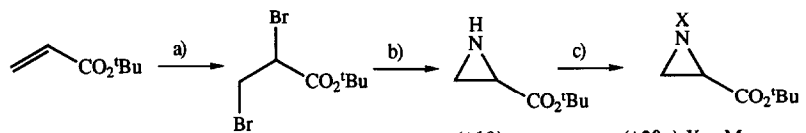
Racemic N-mesyl and N-*iso*-propylsulphonyl aziridine-(2S)-carboxylic acid tbutyl esters (±**20a** and ±**20b**) were synthesised from tbutyl acrylate[23] (Scheme 10) and also subject to the optimised ring opening conditions described above. Both these aziridines displayed analogous behaviour towards copper catalysed Grignard reagents as the N-tosyl compound (**4**) and in each case by-products analogous to **11** and **12** were isolated.



(14b) R = ^{n}Bu **[51%]** $[\alpha]^{D}$ +22.6° (c. 0.45 6N HCl), cf. Lit.[22(ii)] +23.9° (c. 0.04 6N HCl).
(14c) R = ^{i}Pr **[49%]** $[\alpha]^{D}$ +21.0° (c. 0.32 20% w/v HCl).
(14d) R = ^{n}Pr **[46%]** $[\alpha]^{D}$ +22.8° (c. 0.46 6N HCl), cf. Lit.[22(iii)] +23.2° (HCl).
(14e) R = Et **[62%]** $[\alpha]^{D}$ +23.8° (c. 0.75 20% w/v HCl), cf. Lit.[22(iv)] +23.6° (c. 10 20% HCl)
(15a) **[69%]** $[\alpha]^{D}$ -20.0° (c. 0.45 H_2O), cf. Lit.[22(i)] -21° (c. 0.43 H_2O)

Scheme 9

These investigations have demonstrated the use and limitations of stereospecific cuprate ring opening of N-sulphonyl aziridines for the preparation of amino acids in that the production of reduced products **11** and **12** in these reactions compromises the yields obtainable using this method. This problem may be circumvented by the use of N-carbamoyl aziridine-2-carboxylates and will be the subject of future reports.



tert-butyl acrylate (±**18**) (±**19**) (±**20a**) X = Ms
(±**20b**) X = ^{i}PrSO$_2$ **[49%]**

a) Br_2 (1.0 eq), CCl_4, 0°C, 1 h **[100%]**
b) NH_3 (excess) **[76%]**
c) X = Ms: MsCl (1.1 eq), Et_3N (1.1 eq), CH_2Cl_2, 0°C, 1 h **[96%]**
X = ^{i}PrSO$_2$: ^{i}PrSO$_2$Cl (2.0 eq), Et_3N (2.0 eq), CH_2Cl_2, RT, 3 h **[49%]**

Scheme 10

Acknowledgements : A.C.S. thanks the SERC for a 'quota' award and we thank Dr R. M. Adlington for initial studies.

Experimental :*General procedures* : All solvents were distilled before use. 'Petrol' refers to the fraction of light petroleum-ether boiling between 40-60°C. Anhydrous solvents were obtained as follows: CH_2Cl_2, distilled from calcium hydride under argon immediately prior to use, Et_2O and THF, distilled from sodium-benzophenone ketyl under argon and degassed by bubbling argon through for 20 min immediately prior to use, HMPA, dimethoxyethane (DME) and toluene, stirred over calcium hydride under argon for 24 h, distilled under a reduced pressure of argon, and stored over molecular sieves (4Å) under argon, and MeOH, distilled from magnesium methoxide and stored under argon. All the organometallic reagents were used as purchased from Aldrich, as was the copper(I) bromide-dimethylsulfide complex. 1,5-Cyclooctadienyl copper (I) chloride was purchased from Fluka. Flash chromatography was performed on silica gel (Merck Kieselgel 60 F_{254} 230-400 mesh). Preparative layer chromatography (PLC) was performed on glass backed silica plates (200x200x1 mm, 60 F_{254}). TLC was performed on either aluminium or glass backed plates pre-coated with silica (0.2 mm, 60 F_{254}) which were developed using standard visualising agents: UV fluorescence (254 and 366 nm), iodine, ninhydrin / Δ, bromocresol green / Δ, molybdic acid / Δ, anisaldehyde / Δ and vanillin / Δ. R_f values are reported to the

nearest 0.05. Melting points were determined on either Buchi 510 or Gallenkamp capillary apparatus and are uncorrected. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter at 589 nm (Na D-line), and 20 °C, with a path length of 1 dm. Concentrations (c.) are quoted in g / 100 ml. Microanalyses were performed in the Dyson Perrins Laboratory by Mrs. V. Lamburn. Infra red spectra were recorded as thin films, KBr disks, or as solutions in $CHCl_3$, on either a Perkin-Elmer 781 dual beam [calibrated against polystyrene (υ_{max} 1602)] or Perkin-Elmer 1750 fourrier transform spectrometer. Only selected absorbances (υ_{max}) are reported [in wavenumbers (cm^{-1})]. ^1H NMR spectra were recorded at either 200, 250, 300, or 500 MHz on Varian Gemini-200, Bruker AM-250, Bruker WH-300 or Bruker AM-500 instruments, respectively. Chemical shifts (δ_H) are quoted in parts per million (ppm), referenced to the appropriate residual solvent peak. Coupling constants (J) are reported to the nearest 0.5 Hz. ^{13}C NMR spectra were recorded at either 50 or 125 MHz on Varian Gemini-200 or Bruker AM-500 instruments respectively, with DEPT editing. Chemical shifts (δ_C) are quoted in ppm, referenced to the appropriate solvent peak except in the case of spectra recorded in D_2O, which are referenced to 1,4-dioxane. Low resolution mass spectra (m/e) were recorded on V. G. Micromass ZAB 1F (ACE, FAB, CI^+, DCI^+), V. G. Masslab 20-250 (CI^+, DCI^+, EI) and V. G. TRIO 1 (GCMS-CI^+, EI) spectrometers, with only molecular ions (M^+) and major peaks being reported with intensities quoted as percentages of the base peak.

Experimental procedures : N-Triphenylmethyl-(S)-serine methyl ester (**1b**):

To a suspension of (S)-serine methyl ester hydrochloride (**1a**) (15.0 g, 96 mmol) in dichloromethane (200 ml) at 0°C under argon was added dropwise first triethylamine (27.6 ml, 192 mmol, 2.0 eq) and then a solution of triphenylmethyl chloride (27.1 g, 96 mmol, 1.0 eq) in dichloromethane (60 ml). After stirring at 0°C for 12 h the suspended white precipitate (triethylamine hydrochloride) was filtered off under suction and the filtrate evaporated *in vacuo* to yield a white solid which was dissolved in ethyl acetate (100 ml) and washed with $NaHCO_3$ (100 ml, 1.0 M aq.), citric acid (100 ml, 10% w/v aq.) and water (100 ml), dried (Na_2SO_4), filtered and evaporated *in vacuo* to yield the title compound (**1b**) as a white powder which was recrystallised from ethyl acetate-hexane (31.7 g, 91%): R_f (30% ether: hexane) 0.40; mp=77-78°C; $[\alpha]_D^{20}$ +29.9 (c. 1.62, CH_3OH); Found C 76.5, H 6.7, N 4.1%, $C_{23}H_{23}NO_3$ requires C 76.4, H 6.4, N 3.9%; υ_{max} ($CHCl_3$) 3400(w) 3015(m) 1740(s) 1450(s) 1055(s) 905(m) 710(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.40 (1H, bs, NH), 3.00 (1H, bs, OH), 3.31 (3H, s, CO_2CH_3), 3.53-3.63 (2H, m, βHs), 3.69-3.76 (1H, m, αH), 7.16-7.53 (15H, m, ArCH); δ_C (50 MHz, $CDCl_3$) 51.9 (CO_2CH_3), 57.8 (αCH), 65.0 (βCH_2), 70.9 (CPh_3), 126.8, 128.1, 128.9 (ArCH), 145.8 (Ar *ipso*-C), 174.3 (CO_2CH_3); m/e (NH_3 DCI^+) 362 (MH^+, 15%), 243 (CPh_3^+, 100%) 165 (20%), 120 (45%).

N-Triphenylmethyl-O-para-toluenesulphonyl-(S)-serine methyl ester (**1c**):

To a solution of **1b** (25.0 g, 69 mmol) in pyridine (50 ml) at -10°C under argon was added dropwise a solution of *para*-toluenesulphonyl chloride (13.8 g, 76 mmol, 1.1 eq) in pyridine (40 ml), ensuring that the temperature of the solution remained below 0°C. The solution was stirred at 0°C for 8 h and the suspended white precipitate (pyridine hydrochloride) filtered off under suction and the filtrate evaporated *in vacuo*. The resultant brown suspension was dissolved in ethyl acetate (100 ml), washed with copper sulfate (50 ml, 10% w/v aq.), $NaHCO_3$ (50 ml, 1.0 M aq.), citric acid (50 ml, 10% w/v aq.) and water (50 ml), dried (Na_2SO_4), filtered and evaporated *in vacuo* to yield a yellow oil. Chromatography (30% ether: petrol; SiO_2) gave **1c** as a colourless oil (33.5 g, 94%): R_f (30% ether: hexane) 0.20; υ_{max} ($CHCl_3$) 3400(w) 3020(w) 2960(w) 1740(s) 1600(m) 1495(s) 1450(s) 1370(s) 1180(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.47 (3H, s, $ArCH_3$), 2.83 (1H, d, J=10.5 Hz, NH), 3.21 (3H, s, CO_2CH_3), 3.53-3.63 (1H, m, αH), 4.16 (1H, dd, J=6.5, 10.0 Hz, βHH), 4.34 (1H, dd, J=4.5,

10.0 Hz, βHH), 7.17-7.49 (17H, m, ArCH), 7.84 (2H, d, *J*=8.5 Hz, *para*-toluenesulphonyl ArCH); δ_C (50 MHz, $CDCl_3$) 21.5 ($ArCH_3$), 52.1 (CO_2CH_3), 55.4 (αCH), 71.0 (CPh_3), 71.3 (βCH_2), 126.8, 128.1, 128.2, 128.7, 130.0 (ArCH), 133.0, 145 1 (*para*-toluenesulphonyl Ar *ipso*-C), 145.5 (triphenylmethyl Ar -C), 172.2 (CO_2CH_3); m/e (NH_3 DCI$^+$) 516 (MH^+, 100%).

N-Triphenylmethylaziridine-(2S)-carboxylic acid methyl ester (**2a**):

To a solution of **1c** (30.0 g, 87 mmol) in THF (50 ml) under argon was added dropwise triethylamine (16.2 ml, 174 mmol, 2.0 eq). The solution was then refluxed for 14 h, evaporated *in vacuo* and the residue dissolved in ethyl acetate (150 ml). The solution was washed with $NaHCO_3$ (50 ml, 1.0 M aq.), citric acid (50 ml, 10% w/v aq.) and water (100 ml), dried (Na_2SO_4) and filtered to yield a thick brown oil from which **2a** was obtained by recrystallisation from ether (14.4 g, 72%): R_f (10% ether: petrol) 0.30; mp=114-116°C; $[\alpha]_D^{20}$ -89.2 (c. 2.68, THF); Found C 80.8, H 6.6, N 4.1%, $C_{23}H_{21}NO_2$ requires C 80.4, H 6.2, N 4.1%; υ_{max} ($CHCl_3$) 3020(m) 1750(s) 1450(m) 1440(m) 1205(m) 710(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.46 (1H, dd, *J*=6.0, 1.5 Hz, H-3), 1.95 (1H, dd, *J*=6.0, 2.5 Hz, H-2), 2.31 (1H, dd, *J*=1.5, 2.5 Hz, H-3), 3.80 (3H, s, CO_2CH_3), 7.26-7.59 (15H, m, ArCH); δ_C (50 MHz, $CDCl_3$) 28.6 (C-3), 31.6 (C-2), 52.1 (CO_2CH_3), 74.4 (CPh_3), 127.1, 127.9, 129.5 (ArCH),143.8 (Ar *ipso*-C), 172.2 (CO_2CH_3); m/e (NH_3 DCI$^+$) 344 (MH^+, 12%), 243 (CPh_3^+,100%), 165 (13%), 102 (16%).

N-para-Toluenesulphonylaziridine-(2S)-carboxylic acid methyl ester (**2d**):

To a solution of **2a** (3.45 g, 10.0 mmol) in dichloromethane (10 ml) and methanol (12 ml) at -10°C was added trifluoroacetic acid (16 ml) dropwise under argon. After stirring at this temperature for 10 h, water (40 ml) was added and the organic volatiles removed *in vacuo* to precipitate of a mixture of *triphenylmethylcarbinol* [R_f (50% ether: petrol) 0.90; δ_H (200 MHz, $CDCl_3$) 2.95 (1H, bs, OH), 7.22-7.38 (15H, m, ArCH).] and *methoxytriphenylmethane* [R_f (50% ether: petrol) 0.80; δ_H (200 MHz, $CDCl_3$) 3.12 (3H, s, OCH_3), 7.21-7.53 (15H, m, ArCH)] as a white solid which was filtered off prior to evaporation of the aqueous filtrate over ice to yield a pale yellow oil which was azeotroped twice with toluene (2x30 ml) to leave the aziridine salt (**2b**) as a thermolabile, colourless oil [R_f (ethyl acetate) 0.10; δ_H (200 MHz, $CDCl_3$) 2.73 (1H, dd, *J*=4.0, 1.0 Hz, H-3), 2.89 (1H, dd, *J*=1.0, 6.0 Hz, H-3), 3.58 (1H, dd, *J*=4.0, 6.0 Hz, H-2), 3.90 (3H, s, CO_2CH_3), 7.70 (2H, bs, NH_2^+)]. To this salt in dichloromethane (40 ml) at 0°C was added solid potassium carbonate (6.91 g, 50.0 mmol, 5.0 eq), and the solution stirred for 15 min prior to addition of solid *para*-toluenesulphonyl chloride (3.81 g, 2.0 mmol, 2.0 eq) portionwise under argon. The temperature was allowed to rise to ambient and after 2 h the suspended potassium carbonate was filtered off and the filtrate concentrated *in vacuo* to yield a brown viscous oil which was purified by chromatography (40% ether: petrol; SiO_2) to give **2d** as a colourless oil (2.21 g, 86%): R_f (50% ether: petrol) 0.30; $[\alpha]_D^{20}$ -55.2 (c. 1.17, $CHCl_3$); Found C 51.8, H 5.3, N 5.6%, $C_{11}H_{13}NO_4S$ requires C 51.8, H 5.1, N 5.5%; υ_{max} ($CHCl_3$) 3015(m) 1748(s) 1600(m) 1440(s) 1335(s) 1165(s) 910(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.43 (3H, s, $ArCH_3$), 2.54 (1H, d, *J*=4.0 Hz, H-3), 2.74 (1H, d, *J*=7.0 Hz, H-3), 3.32 (1H, dd, *J*=4.0, 7.0 Hz, H-2), 3.71 (3H, s, CO_2CH_3), 7.34 (2H, d, *J*=8.0 Hz, ArCH), 7.82 (2H, d, *J*=8.0 Hz, ArCH); δ_C (50 MHz, $CDCl_3$) 21.5 ($ArCH_3$), 31.9 (C-3), 35.5 (C-2), 52.8 (CO_2CH_3), 128.3, 130.0 (ArCH), 134.0, 145.5 (Ar *ipso*-C), 167.4 (CO_2CH_3); m/e (NH_3 CI$^+$) 273 (MNH_4^+, 100%), 256 (MH^+, 30%).

N-para-Toluenesulphonylaziridine-(2S)-carboxylic acid (**3**):

The methyl ester (**2d**) (3.64 g, 14.3 mmol) was dissolved in 1,4-dioxane (16 ml) and cooled to 0°C and a solution of lithium hydroxide monohydrate (658 mg, 15.7 mmol, 1.1 eq) in water (4 ml) was added dropwise. After 15 min the 1,4-dioxane was removed *in vacuo* and the aqueous solution extracted with dichloromethane (2x20 ml). The aqueous phase was neutralised with citric acid (10% w/v aq.), re-extracted with dichloromethane (3x20 ml) and the combined organic extracts dried ($MgSO_4$), filtered and concentrated *in vacuo* to yield the title acid (**3**) as a pale brown oil (3.30 g, 96%): R_f (50% ether: petrol) 0.10; υ_{max} ($CHCl_3$) 3015(s) 2960(s) 2690(w) 2580(w) 1730(s) 1600(m) 930(m) 690(m) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.41 (3H, s, ArC<u>H</u>$_3$), 2.51 (1H, d, *J*=4.0 Hz, <u>H</u>-3), 2.76 (1H, d, *J*=6.0 Hz, <u>H</u>-3), 3.27 (1H, dd, *J*=4.0, 6.0 Hz, <u>H</u>-2), 7.31 (2H, d, *J*=7.0 Hz, ArC<u>H</u>), 7.80 (2H, d, *J*=7.0 Hz, ArC<u>H</u>), 10.3 (1H, bs, CO_2<u>H</u>); δ_C (50 MHz, $CDCl_3$) 21.5 (Ar<u>C</u>H$_3$), 32.1 (<u>C</u>-3), 35.4 (<u>C</u>-2), 128.3, 130.1 (Ar<u>C</u>H), 133.7, 145.7 (Ar *ipso*-<u>C</u>), 171.5 (<u>C</u>O_2H); m/e (NH_3 DCI$^+$) 259 (MNH_4^+, 100%), 242 (MH^+, 50%), 192 (30%), 139 (12%), 108 (13%), 91 (12%).

N-para-Toluenesulphonylaziridine-(2<u>S</u>)-carboxylic acid tert-butyl ester (**4**):

To a solution of the acid (**3**) (2.01 g, 8.3 mmol) in dichloromethane (8 ml) was added a solution of *tert*-butyl trichloroacetimidate (3.64 g, 16.6 mmol, 2.0 eq) in cyclohexane (16 ml) under argon. Boron trifluoride etherate (200 µl, cat.) was then added dropwise and a white precipitate ensued. After stirring for 10 min the reaction was quenched with solid $NaHCO_3$ (0.70 g, 8.3 mmol, 1.0 eq) and the solution filtered through a plug of Celite® concentrated *in vacuo* and purified by chromatography (20% ether: petrol; SiO_2) to yield **4** as a white crystalline solid (2.13 g, 86%): R_f (50% ether: petrol) 0.80; mp=74-75°C; $[\alpha]_D^{20}$ -45.0 (c. 1.09, CH_2Cl_2); Found C 56.4, H 6.7, N 4.6%, $C_{14}H_{19}NO_4S$ requires C 56.5, H 6.4, N 4.7%; υ_{max} ($CHCl_3$) 3520(m) 2990(m) 1740(s) 1600(m) 1165(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.44 (9H, s, C(C<u>H</u>$_3$)$_3$), 2.47 (3H, s, ArC<u>H</u>$_3$), 2.51 (1H, d, *J*=4.0 Hz, <u>H</u>-3), 2.71 (1H, d, *J*=7.0 Hz, <u>H</u>-3), 3.24 (1H, dd, *J*=4.0, 7.0 Hz, <u>H</u>-2), 7.37 (2H, d, *J*=8.0 Hz, ArC<u>H</u>), 7.87 (2H, d, *J*=8.0 Hz, ArC<u>H</u>); δ_C (50 MHz, $CDCl_3$) 21.5 (Ar<u>C</u>H$_3$), 27.7 (C(<u>C</u>H$_3$)$_3$), 31.8 (<u>C</u>-3), 36.7 (<u>C</u>-2), 83.1 (<u>C</u>(CH$_3$)$_3$), 128.3, 130.0 (Ar<u>C</u>H), 134.3, 145.4 (Ar *ipso*-<u>C</u>), 166.0 (<u>C</u>O_2^{t}Bu); m/e (NH_3 CI$^+$) 315 (MNH_4^+, 57%), 298 (MH^+, 44%), 259 (MNH_5^+-^{t}Bu, 100%), 242 (MH_2^+-^{t}Bu, 90%).

N-para-Toluenesulphonyl dehydroalanine methyl ester (**5**):

(<u>S</u>)-Serine methyl ester hydrochloride (**1a**) (1.56 g, 10.0 mmol) was added in portions to a solution of *para*-toluenesulphonyl chloride (4.80 g, 25.0 mmol, 2.5 eq) in pyridine (60 ml) at 0-5°C afterwhich the solution was allowed to warm to ambient temperature under argon over 13 h. The pyridine was removed *in vacuo* and the residual brown paste re-dissolved in ethyl acetate (50 ml), washed with copper sulfate (2x20 ml, 10% w/v aq.), acetic acid (20 ml, 10% w/v aq.) and water (50 ml). The organic phase was dried (Na_2SO_4), filtered, concentrated *in vacuo* and purified by chromatography (40% ether: petrol; SiO_2) to yield **5** as a white powder (0.46 g, 20%): R_f (40% ether: petrol) 0.30; mp=93-94°C; Found C 51.7, H 5.1, N 5.3, S 12.5%, $C_{11}H_{13}NO_4S$ requires C 51.7, H 5.1, N 5.3, S 12.6%; υ_{max} (CCl_4) 3360(s) 2960(m) 1725(s) 1640(s) 1600(w) 1450(s) 1425(s) 1290(s) 1175(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.42 (3H, s, ArC<u>H</u>$_3$), 3.76 (3H, s, CO_2C<u>H</u>$_3$), 5.66 (2H, d, *J*=6.0 Hz, β<u>H</u>'s), 7.16 (1H, bs, N<u>H</u>), 7.30 (2H, d, *J*=8.5 Hz, ArC<u>H</u>), 7.75 (2H, d, *J*=8.5 Hz, ArC<u>H</u>); δ_C (50 MHz, $CDCl_3$) 21.4 (Ar<u>C</u>H$_3$), 53.1 (CO_2<u>C</u>H$_3$), 107.0 (β<u>C</u>H$_2$), 127.7, 129.8 (Ar<u>C</u>H), 131.0 (α<u>C</u>H), 135.5, 144.5 (Ar *ipso*-<u>C</u>), 163.9 (<u>C</u>O_2CH$_3$); m/e (NH_3 ACE) 273 (MNH_4^+, 96%), 256 (MH^+, 100%), 191 (30%), 102 (50%).

N-para-Toluenesulphonyl-(<u>S</u>)-serine methyl ester (**1d**):

To a suspension of (S)-serine methyl ester hydrochloride (**1a**) (4.76 g, 30 mmol) in dichloromethane (50 ml) at 0°C under argon was added dropwise first triethylamine (8.36 ml, 60 mmol, 2.0 eq) and then a solution of *para*-toluenesulphonyl chloride (5.72 g, 30 mmol, 1.0 eq) in dichloromethane (10 ml). After stirring at 0°C for 12 h the suspended white precipitate (triethylamine hydrochloride) was filtered off under suction and the filtrate evaporated *in vacuo* to yield a white solid. This was dissolved in ethyl acetate (50 ml), washed with $NaHCO_3$ (40 ml, 1.0 M aq.), citric acid (40 ml, 10% w/v aq.) and water (40 ml) and then dried (Na_2SO_4), filtered and evaporated to yield the title compound (**1d**) as a white powder which was recrystallised from ethyl acetate-hexane (6.20 g, 76%): R_f (70% ether: hexane) 0.10; mp=84-85°C; $[\alpha]_D^{20}$ +12.2 (c. 0.83, $CHCl_3$); Found C 48.5, H 5.6, N 5.2, S 11.4%, $C_{11}H_{15}NO_5S$ requires C 48.3, H 5.5, N 5.1, S 11.7%; υ_{max} ($CHCl_3$) 3330(w) 3030(m) 1742(s) 1600(w) 1350(s) 1155(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.40 (3H, s, $ArCH_3$), 2.98 (1H, bs, OH), 3.58 (3H, s, CO_3CH_3), 3.85-3.92 (2H, m, βH's), 3.95-4.03 (1H, m, αH), 5.99 (1H, d, *J*=8.0 Hz, NH), 7.29 (2H, d, *J*=8.5 Hz, Ar CH), 7.75 (2H, d, *J*=8.5 Hz, Ar CH); δ_C (50 MHz, $CDCl_3$) 21.4 ($ArCH_3$), 52.8 (CO_2CH_3), 57.6 (αCH), 63.6 (βCH_2), 127.3, 129.9 (ArCH), 136.7, 144.0 (Ar *ipso*-C), 170.6 (CO_2CH_3); m/e (NH_3 DCI$^+$) 291 (MNH_4^+, 100%), 274 (MH^+, 30%).

N-para-Toluenesulphonyl-O-methanesulphonyl-(S)-serine methyl ester (**1e**):

To a solution of N-*para*-toluenesulphonyl-(S)-serine methyl ester (**1d**) (2.50 g, 9.2 mmol) in THF (35 ml) at 0°C under argon was added dropwise first triethylamine (1.41 ml, 10.1 mmol, 1.1 eq) and then methanesulphonyl chloride (1.07 ml, 13.7 mmol, 1.5 eq). After stirring at ambient temperature for 3 h the suspended white precipitate was filtered off under suction and the filtrate evaporated *in vacuo*. The residue was dissolved in ethyl acetate (30 ml) and washed with $NaHCO_3$ (20 ml, 1.0 M aq.) and brine (20 ml) then dried ($MgSO_4$), filtered and evaporated *in vacuo* to yield **1e** as a white powder which was recrystallised from dichloromethane-hexane (2.81 g, 87%): R_f (50% ethyl acetate: hexane) 0.30; mp=141-142°C; $[\alpha]_D^{20}$ +58.6 (c. 1.23, CH_3COCH_3); Found C 41.1, H 4.9, N 4.0, S 18.3%, $C_{12}H_{17}NO_7S_2$ requires C 41.0, H 4.9, N 4.0, S 18.3%; υ_{max} ($CHCl_3$) 3330(w) 3030(w) 2960(m) 1750(s) 1370(s) 1350(s) 1180(s) 1170(s) cm^{-1}; δ_H (200 MHz, CD_3COCD_3) 2.40 (3H, s, $ArCH_3$), 3.07 (3H, s, SO_2CH_3), 3.54 (3H, s, CO_3CH_3), 4.34-4.50 (3H, m, α+βH's), 7.22 (1H, d, *J*=8.0 Hz, NH), 7.38 (2H, d, *J*=8.0 Hz, Ar CH), 7.76 (2H, d, *J*=8.5 Hz, Ar CH); δ_C (125 MHz, CD_3COCD_3) 21.4 ($ArCH_3$), 37.3 (SO_2CH_3), 53.0 (CO_2CH_3), 56.1 (αCH), 70.4 (βCH_2), 127.9, 130.4 (ArCH), 139.1, 144.3 (Ar *ipso*-C), 169.2 (CO_2CH_3); m/e (NH_3 DCI$^+$) 369 (MNH_4^+, 32%), 273 (100%), 256 (60%), 102 (31%).

Ring-closure of N-para-toluenesulphonyl-O-methanesulphonyl-(S)-serine methyl ester (**1e**):

To a suspension of potassium carbonate (118 mg, 0.85 mmol, 1.5 eq) in methanol (2 ml) under argon at 0°C was added a solution of **1e** (200 mg, 0.57 mmol) in methanol dropwise (2 ml). After 15 min at 0°C the solution was poured onto ice (*ca.* 30 g) and the resultant solution extracted with dichloromethane (4x20 ml). The organic extracts were combined, dried ($MgSO_4$), filtered and concentrated *in vacuo* to yield a yellow oil (140 mg). Proton NMR at 200 MHz in deutero-chloroform revealed the crude product to be composed of **5** and **2d** in a *ca.* 2: 1 ratio.

Reaction of N-para-toluenesulphonylaziridine-(2S)-carboxylic acid tert-butyl ester (**4**) *with n-butyl lithium:*

Table 1, entry 1: To a solution of **4** (153 mg, 0.51 mmol) in DME (2 ml) under argon at -78°C was added n-butyl lithium (605 µl, 1.53 M soln. in hexanes, 0.92 mmol, 1.8 eq) dropwise. After stirring at this temperature for 15 min the reaction was quenched with cold water (5 ml) and stirred for 10 min before separation of the phases; the aqueous phases were re-extracted with dichloromethane (3x15 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated *in vacuo* to yield a pale yellow oil (139 mg). Purification by PLC (50% ether: petrol; SiO_2) gave:

R_f (50% ether: petrol) 0.70: (**4**) (48mg, 31%).

R_f (50% ether: petrol) 0.50: *(2S)-2-[pentan-1'-one]N-para-toluenesulphonylaziridine* (**6**) (30 mg, 21%), colourless oil: υ_{max} ($CHCl_3$) 3020(s) 2960(m) 2940(m) 1720(s) 1600(w) 1345(s) 1165(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.84 (3H, t, *J*=7.0 Hz, $(CH_2)_3CH_3$), 1.13-1.62 (6H, m, $(CH_2)_3CH_3$), 2.38 (1H, d, *J*=4.0 Hz, H-3), 2.47 (3H, s, $ArCH_3$), 2.78 (1H, d, *J*=7.5 Hz, H-3), 3.32 (1H, dd, *J*=4.0, 7.5 Hz, H-2), 7.37 (2H, d, *J*=8.0 Hz, ArCH), 7.84 (2H, d, *J*=8.0 Hz, ArCH); δ_C (125 MHz, $CDCl_3$) 13.7 ($(CH_2)_3CH_3$), 21.1 ($ArCH_3$), 25.2, 29.7, 38.9 ($(CH_2)_3CH_3$), 31.9 (C-3), 41.3 (C-2), 128.2, 129.9 (ArCH), 134.1, 145.3 (Ar *ipso*-C), 203.5 (CO^nBu); m/e (NH_3 CI^+) 299 (MNH_4^+, 10%), 282 (MH^+, 100%) 189 (94%), 155 (32%), 111 (41%).

R_f (50% ether: petrol) 0.45: *(2S)-2-(1'-butan-pentan-1'-ol)N-para-toluenesulphonylaziridine* (**7a**) (92 mg, 43%), white crystalline solid: mp=94-95°C; υ_{max} ($CHCl_3$) 3565(w) 3020(s) 2960(m) 2940(m) 2400(w) 1600(w) 1325(s) 1160(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.79-0.93 (6H, m, 2x$(CH_2)_3CH_3$), 1.09-1.47 (12H, m, 2x$(CH_2)_3CH_3$), 2.42 (1H, d, *J*=4.5 Hz, H-3), 2.45 (3H, s, $ArCH_3$), 2.60 (1H, d, *J*=7.0 Hz, H-3), 2.81 (1H, dd, *J*=4.5, 7.0 Hz, H-2), 7.35 (2H, d, *J*=8.0 Hz, ArCH), 7.84 (2H, d, *J*=8.0 Hz, ArCH); δ_C (125 MHz, $CDCl_3$) 13.8, 13.9 (2x$(CH_2)_3CH_3$), 21.6 ($ArCH_3$), 23.0, 23.2, 25.2, 25.2, 35.8, 39.5 (2x$(CH_2)_3CH_3$), 30.2 (C-3), 46.0 (C-2), 70.7 (COH), 128.2, 129.7 (ArCH), 134.9, 144.8 (Ar *ipso*-C); m/e (NH_3 CI^+) 357 (MNH_4^+, 8%), 340 (MH^+, 100%) 322 (98%), 282 (20%), 186 (64%).

Reaction of N-para-toluenesulphonylaziridine-(2S)-carboxylic acid tert-butyl ester (**4**) *with methyl Grignard reagent*:

Table 1, entry 2: To a solution of aziridine **4** (100 mg, 0.34 mmol) in THF (3 ml) under argon at -78°C was added methyl magnesium chloride (348 µl, 3.0 M soln. in THF, 1.05 mmol, 3.1 eq) dropwise. After 10 min at -78°C the solution was warmed to ambient temperature during 1 h and then refluxed for 30 min. The solution was cooled, quenched with cold water (10 ml) and stirred for 15 min. Aqueous workup as above yielded a yellow oil (61 mg) which was purified by PLC (as entry 1) to give *1-methyl-(2S-N-para-toluenesulphonylamino) pentan-1-ol* (**8**), colourless oil (58 mg, 64%): υ_{max} (neat) 3510(m) 2980(s) 1600(m) 1340(s) 1160(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.63 (3H, t, *J*=7.5 Hz, C(5)H_3), 1.15 (3H, s, CH_3), 1.17 (3H, s, CH_3), 1.56-1.69 (2H, m, C(4)H_2), 2.22 (1H, bs, OH), 2.43 (3H, s, $ArCH_3$), 3.07 (1H, dt, *J*=3.5, 9.5 Hz, H-3), 4.62 (1H, d, *J*=8.5 Hz, NH), 7.30 (2H, d, *J*=8.0 Hz, Ar CH), 7.78 (2H, d, *J*=8.0 Hz, Ar CH); δ_C (50 MHz, $CDCl_3$) 10.8 (C-4), 21.4 ($ArCH_3$), 24.0, 25.1 (2xCH_3), 27.4 (C-4), 64.8 (C-3), 72.6 (C-2), 127.3, 129.8 (ArCH), 138.2, 143.6 (Ar *ipso*-C); m/e (NH_3 CI^+) 289 (MNH_4^+, 14%), 272 (MH^+, 35%), 254 (100%), 242 (20%), 212 (18%).

Table 1, entry 3: To a solution of aziridine **4** (110 mg, 0.37 mmol) in THF (2 ml) under argon at -78°C was added methyl magnesium chloride (136 µl, 3.0 M soln. in THF, 0.41 mmol, 1.1 eq) dropwise. The solution was warmed to ambient temperature, stirred for 5 h, quenched with NH_4Cl (5 ml, sat. aq.) and concentrated *in vacuo*. The residue was partitioned between ether (20 ml) and water (20 ml) and the organic phase washed with

brine (20 ml), dried ($MgSO_4$), filtered and concentrated *in vacuo* to yield a colourless oil. Purification by PLC (as entry 1) gave:

R_f (50% ether: petrol) 0.70: (**4**) (55 mg, 50%).

R_f (50% ether: petrol) 0.40: *(2S)-2-(1'methylethan-1'-ol)N-para-toluenesulphonylaziridine* (**7b**) (36 mg, 38%), colourless oil; υ_{max} ($CHCl_3$) 3567(w) 3020(s) 2960(m) 2940(m) 2400(w) 1600(w) 1330(s) 1165(s) 940(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.15 (3H, s, CH_3), 1.21 (3H, s, CH_3), 1.63 (1H, bs, OH), 2.40 (1H, d, *J*=4.5 Hz, H-3), 2.48 (3H, s, $ArCH_3$), 2.60 (1H, d, *J*=7.0 Hz, H-3), 2.82 (1H, dd, *J*=4.5, 7.0 Hz, H-2), 7.38 (2H, d, *J*=8.0 Hz, ArCH), 7.86 (2H, d, *J*=8.0 Hz, ArCH); δ_C (125 MHz, $CDCl_3$) 21.6 ($ArCH_3$), 25.4, 28.4 ($2xCH_3$), 30.5 (C-3), 47.4 (C-2), 67.3 (COH), 128.2, 129.7 (ArCH), 134.8, 144.8 (Ar *ipso*-C); m/e (NH_3 CI^+) 273 (MNH_4^+, 32%), 256 (MH^+, 100%) 189 (29%), 102 (34%).

Table 1, entry 4 : To a solution of aziridine **4** (110 mg, 0.37 mmol) in THF (2 ml) under an argon at -78°C was added methyl magnesium chloride (383 µl, 3.0 M soln. in THF, 1.15 mmol, 3.1 eq) dropwise. The solution was warmed to ambient temperature, stirred for 19 h and then quenched and worked up as above to yield a colourless oil. Purification by PLC (as entry 1) gave **7b** (57 mg, 60%) and **8** (20 mg, 20%).

Reaction of N-para-toluenesulphonylaziridine-(2S)-carboxylic acid tert-butyl ester (**4**) *with 'higher-order' cuprates* :

Table 2, entry 1: Copper (I) cyanide powder (vacuum desiccated over phosphorus pentoxide, 76 mg, 0.85 mmol, 1.2 eq) was placed in an oven dried, two neck flask equipped with an efficient stirrer. The flask was purged with argon prior to addition of ether (1 ml) and the resultant suspension cooled to -78°C before the addition of methyl lithium (1.26 ml, 1.35 M soln. in THF, 1.70 mmol, 2.4 eq). The suspension was warmed to ambient temperature over *ca.* 15 min to give a homogeneous pale green solution of the cuprate which was re-cooled to -78°C prior to addition of aziridine **4** (210 mg, 0.71 mmol) as a solution in THF (1 ml) dropwise. After *ca.* 10 min the solution became yellow and the reaction was quenched with cold water (5 ml), partitioned between dichloromethane (20 ml) and NH_4Cl (10 ml, sat. aq.) and the aqueous phase re-extracted with dichloromethane (3x20 ml); the combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo* to yield a thick brown oil (153 mg). A 50 mg portion of the crude product was purified by PLC (50% ether: petrol; SiO_2) to give four isolated compounds:

R_f (50% ether: petrol) 0.50: *N-para-toluenesulphonyl-(2S)-aminobutanoic acid tert-butyl ester* (**9a**) (20%), white crystalline solid: mp=104-106°C; Found C 57.5, H 7.3, N 4.8, S 10.3%, $C_{15}H_{23}NO_4S$ requires C 57.5, H 7.4, N 4.5, S 10.2%; υ_{max} ($CHCl_3$) 3340(w) 3020(m) 1730(s) 1350(m) 1165(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.93 (3H, t, *J*=7.5 Hz, C(4)H_3), 1.25 (9H, s, $C(CH_3)_3$), 1.52-1.82 (2H, m, βH's), 2.40 (3H, s, $ArCH_3$), 3.73 (1H, ddd, *J*=5.0, 7.0, 9.0 Hz, αH), 5.13 (1H, d, *J*=9.0 Hz, NH), 7.29 (2H, d, *J*=8.0 Hz, ArCH), 7.73 (2H, d, *J*=8.5 Hz, ArCH); δ_C (125 MHz, $CDCl_3$) 9.2 (C-4), 21.4 ($ArCH_3$), 26.9 (βCH_2), 27.7 ($C(CH_3)_3$), 57.2 (αCH), 82.3 ($C(CH_3)_3$), 127.3, 129.6 (ArCH), 137.0, 143.5 (Ar *ipso*-C), 170.7 ($CO_2{}^tBu$); m/e (NH_3 CI^+) 331 (MNH_4^+, 53%), 314 (MH^+, 4%) 275 (MNH_5^+-^{t}Bu, 100%), 258 (MH_2^+-^{t}Bu, 41%), 212 (55%).

R_f (50% ether: petrol) 0.40: *(2R)-(N-para-toluenesulphonylamino)-2-methylpropanoic acid tert-butyl ester* (**10a**) (20%), yellow oil: Found C 57.2, H 7.4, N 4.7, S 10.0%, $C_{15}H_{23}NO_4S$ requires C 57.5, H 7.4, N 4.5, S 10.2%; υ_{max} ($CHCl_3$) 3340(w) 3020(m) 2980(m) 1730(s) 1335(m) 1160(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.12 (3H, d, *J*=7.5 Hz, C(4)H_3), 1.42 (9H, s, $C(CH_3)_3$), 2.44 (3H, s, $ArCH_3$), 2.48-2.62 (1H, m, C(2)H), 2.89-

3.18 (2H, m, C$\underline{H}_2$), 5.06 (1H, t, *J*=6.5 Hz, N$\underline{H}$), 7.32 (2H, d, *J*=8.0 Hz, ArC$\underline{H}$), 7.75 (2H, d, *J*=8.0 Hz, ArC$\underline{H}$); δ_C (125 MHz, $CDCl_3$) 15.0 ($\underline{C}$-3), 21.5 (Ar$\underline{C}H_3$), 28.0 (C($\underline{C}H_3$)$_3$), 40.2 ($\underline{C}$-2), 45.5 (C(2)$\underline{C}H_2$), 81.3 ($\underline{C}$(CH$_3$)$_3$), 127.0, 129.7 (Ar$\underline{C}$H), 137.1, 143.3 (Ar *ipso*-$\underline{C}$), 174.3 ($\underline{C}O_2$^{t}Bu); m/e (NH_3 CI$^+$) 331 (MNH_4^+, 53%), 314 (MH^+, 11%) 275 (MNH_5^+-^{t}Bu, 100%), 258 (MH_2^+-^{t}Bu, 80%), 102 (30%).

R_f (50% ether: petrol) 0.40: *para-toluenesulphonamide* (7%), white crystalline solid: mp=138-139°C; δ_H (200 MHz, $CDCl_3$) 2.46 (3H, s, Ar$\underline{C}H_3$), 4.74 (2H, bs, N$\underline{H}_2$), 7.32 (2H, d, *J*=8.0 Hz, ArC$\underline{H}$), 7.81 (2H, d, *J*=8.0 Hz, ArC$\underline{H}$); m/e (NH_3 CI$^+$) 189 (MNH_4^+, 100%) 108 (21%)

R_f (50% ether: petrol) 0.05: *4-(N-para-toluenesulphonylamino)butan-2-one* (**11**) (40%), colourless oil: υ_{max} (neat) 3350(w) 3015(m) 1718(s) 1600(w) 1340(s) 1165(s) 1095(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.12 (3H, s, C(1)$\underline{H}_3$), 2.44 (3H, s, Ar$\underline{C}H_3$), 2.70 (2H, t, *J*=5.5 Hz, C(3)$\underline{H}_2$), 3.14 (2H, dd, *J*=6.5, 12.0 Hz, C(4)$\underline{H}_2$), 5.13 (1H, t, *J*=6.5 Hz, N$\underline{H}$), 7.31 (2H, d, *J*=8.0 Hz, Ar C$\underline{H}$), 7.74 (2H, d, *J*=8.5 Hz, Ar C$\underline{H}$); δ_C (125 MHz, $CDCl_3$) 21.5 (Ar$\underline{C}H_3$), 30.0 ($\underline{C}$-3), 38.0 ($\underline{C}$-1), 42.9 ($\underline{C}$-4), 127.0, 129.7 (Ar$\underline{C}$H), 137.0, 143.4 (Ar *ipso*-$\underline{C}$), 207.8 ($\underline{C}$OCH$_3$); m/e (NH_3 CI$^+$) 259 (MNH_4^+, 72%), 242 (100%), 86 (60%).

Table 2, entry 2: To a suspension of copper (I) cyanide (73 mg, 0.82 mmol, 1.2 eq) in THF (1 ml) at -78°C was added n-butyl lithium (1.06 ml, 1.53 M soln. in hexanes, 1.64 mmol, 2.4 eq) dropwise. The suspension was warmed to ambient temperature over *ca.* 15 min to give a homogeneous brown solution of the cuprate which was re-cooled to -78°C prior to dropwise addition of aziridine **4** (200 mg, 0.67 mmol) in THF (1.5 ml). After 4.5 h the reaction was quenched with cold water (15 ml). The crude solution was filtered to remove precipitated copper salts and the aqueous filtrate extracted with dichloromethane (3x20 ml); the combined organic phases were dried ($MgSO_4$), filtered and concentrated *in vacuo* to yield a thick brown oil (131 mg). Purification by PLC (as entry 1) gave:

R_f (50% ether: petrol) 0.70: *(2S)-N-para-toluenesulphonylaminoheptanoic acid tert-butyl ester* (**9b**) (66 mg, 28%), white crystalline solid: mp=85-87°C; $[\alpha]_D^{20}$ +23.2 (c. 0.99, CH_2Cl_2); Found C 61.1, H 8.4, N 3.8%, $C_{18}H_{29}NO_4S$ requires C 60.8, H 8.2, N 3.9%; υ_{max} ($CHCl_3$) 3340(w) 3020(m) 2960(m) 2940(m) 1730(s) 1350(m) 1165(s) cm^{-1}; δ_H (250 MHz, $CDCl_3$); 0.87 (3H, t, *J*=7.0 Hz, C(7)$\underline{H}_3$), 1.26 (9H, s, C(C$\underline{H}_3$)$_3$), 1.26-1.36 (6H, m, 3 x C$\underline{H}_2$), 1.55-1.75 (2H, m, $\beta\underline{H}$'s), 2.41 (3H, s, Ar$\underline{C}H_3$), 3.77 (1H, ddd, *J*=5.0, 7.5, 9.0 Hz, $\alpha\underline{H}$), 5.09 (1H, d, *J*=9.5 Hz, N$\underline{H}$), 7.28 (2H, d, *J*=8.0 Hz, ArC$\underline{H}$), 7.73 (2H, d, *J*=8.5 Hz, ArC$\underline{H}$); δ_C (125 MHz, $CDCl_3$) 13.9 ($\underline{C}$-7), 21.4 (Ar$\underline{C}H_3$), 22.3, 24.4, (2x$\underline{C}H_2$), 27.7 (C($\underline{C}H_3$)$_3$), 31.2, 33.6 (2x$\underline{C}H_2$), 56.2 ($\alpha\underline{C}$H), 82.2 ($\underline{C}$(CH$_3$)$_3$), 127.3, 129.6 (Ar$\underline{C}$H), 137.2, 143.4 (Ar *ipso*-$\underline{C}$), 171.0 ($\underline{C}O_2$^{t}Bu); m/e (NH_3 DCI$^+$) 373 (MNH_4^+, 50%), 356 (MH^+, 4%) 317 (MNH_5^+-^{t}Bu, 100%), 300 (MH_2^+-^{t}Bu, 38%), 254 (64%), 243 (25%).

R_f (50% ether: petrol) 0.70: (**4**) (56 mg, 28%).

R_f (50% ether: petrol) 0.60: *(2R)-(N-para-toluenesulphonylaminomethyl)hexanoic acid tert-butyl ester* (**10b**) (36 mg, 15%), colourless oil: υ_{max} ($CHCl_3$) 3340(w) 3020(m) 2960(m) 2940(m) 2980(m) 1715(s) 1335(m) 1160(s) cm^{-1}; δ_H (250 MHz, $CDCl_3$) 0.88 (3H, t, *J*=7.0 Hz, C(6)$\underline{H}_3$), 1.20-1.60 (6H, m, 3 x C$\underline{H}_2$), 1.43 (9H, s, C(C$\underline{H}_3$)$_3$), 2.44 (3H, s, Ar$\underline{C}H_3$), 2.40-2.44 (1H, m, C(2)$\underline{H}$), 3.05 (2H, dd, *J*=6.0, 10.0 Hz, C(2)C$\underline{H}_2$), 4.94 (1H, t, *J*=7.0 Hz, N$\underline{H}$), 7.32 (2H, d, *J*=7.5 Hz, ArC$\underline{H}$), 7.75 (2H, d, *J*=8.0 Hz, ArC$\underline{H}$); δ_C (125 MHz, $CDCl_3$) 13.6 ($\underline{C}$-6), 21.3 (Ar$\underline{C}H_3$), 22.3 ($\underline{C}H_2$), 27.9 (C($\underline{C}H_3$)$_3$), 28.7, 29.2, (2x$\underline{C}H_2$), 43.7 (C(2)$\underline{C}H_2$), 45.5 ($\underline{C}$-2), 81.3 ($\underline{C}$(CH$_3$)$_3$), 127.1, 129.8 (Ar$\underline{C}$H), 137.1, 143.5 (Ar *ipso*-$\underline{C}$), 174.3 ($\underline{C}O_2$^{t}Bu); m/e (NH_3 CI$^+$) 373 (MNH_4^+, 50%), 356 (MH^+, 8%) 317 (MNH_5^+-^{t}Bu, 100%), 300 (MH_2^+-^{t}Bu, 64%), 144 (25%).

R_f (50% ether: petrol) 0.40: *3-(N-para-toluenesulphonylamino)propanoic acid tert-butyl ester* (**12**) (30 mg, 15%), colourless oil: υ_{max} ($CHCl_3$) 3340(w) 3020(m) 2960(m) 2940(m) 1720(s) 1340(m) 1160(s) cm^{-1}; δ_H (500 MHz, $CDCl_3$); 1.43 (9H, s, $C(C\underline{H}_3)_3$), 2.44 (3H, s, $ArC\underline{H}_3$), 2.44 (2H, t, *J*=6.5 Hz, $C(2)\underline{H}_2$), 3.15 (2H, dt, *J*=6.5, 6.5 Hz, $C(3)\underline{H}_2$), 5.15 (1H, t, *J*=6.5 Hz, $N\underline{H}$), 7.28 (2H, d, *J*=8.0 Hz, $ArC\underline{H}$), 7.73 (2H, d, *J*=8.5 Hz, $ArC\underline{H}$); δ_C (125 MHz, $CDCl_3$) 21.5 ($Ar\underline{C}H_3$), 28.0 ($C(\underline{C}H_3)_3$), 34.9, 38.9 ($2x\underline{C}H_2$), 81.6 ($\underline{C}(CH_3)_3$), 127.0, 129.7 ($Ar\underline{C}H$), 137.1, 143.4 (Ar *ipso*-$\underline{C}$), 171.4 ($\underline{C}O_2{}^tBu$); m/e (NH_3 CI^+) 317 (MNH_4^+, 23%), 300 (MH^+, 7%) 261 (MNH_5^+-^{t}Bu, 100%), 244 (MH_2^+-^{t}Bu, 66%), 88 (38%).

Table 2, entry 3: To a suspension of copper (I) cyanide (67 mg, 0.75 mmol, 1.1 eq) in ether (1 ml) at -78°C was added n-butyl lithium (976 µl, 1.53 M soln. in hexanes, 1.47 mmol, 2.2 eq) dropwise. The suspension to was warmed to ambient temperature over *ca.* 15 min, then re-cooled to -78°C and aziridine **4** (200 mg, 0.67 mmol) added dropwise as a solution in 60% toluene: ether (1.5 ml). After 20 min at -78°C the reaction was quenched with NH_4Cl (15 ml, sat. aq.), stirred for 15 min and then extracted with ether (3x20 ml). The combined organic phases were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give a thick brown oil (187 mg). Purification by PLC (as entry 1) gave **9b**(59 mg, 25%), **4** (102 mg, 51%), **10b** (14 mg, 6%) and **12** (24 mg, 12%).

Table 2, entry 4: To a suspension of copper (I) cyanide (65 mg, 0.73 mmol, 1.1 eq) in ether (1 ml) at -78°C was added n-butyl lithium (952 µl, 1.53 M soln. in hexanes, 1.46 mmol, 2.2 eq) dropwise. The suspension was warmed to ambient temperature over *ca.* 15 min, then re-cooled to -78°C and aziridine **4** (198 mg, 0.67 mmol) added dropwise as a solution in 60% toluene: ether (1.5 ml). The solution was allowed to warm slowly to ambient temperature over 22 h and was then quenched and worked up as above to yield a yellow oil (253 mg). Purification by PLC (as entry 1) gave **9b** (71 mg, 30%), **4** (80 mg, 40%), **10b** (26 mg, 11%) and **12** (22 mg, 11%).

Reaction of N-para-toluenesulphonylaziridine-(2S)-carboxylic acid tert-butyl ester (**4**) *with copper catalysed Grignard reagents*:

Table 3, entry 1: To a solution of aziridine 4 (50 mg, 0.17 mmol) in THF (4.5 ml) was added dimethylsulfide (500 µl) and $CuBr.SMe_2$ (9 mg, 0.034 mmol, 0.2 eq). The resultant homogenous solution was cooled to -30°C and methyl magnesium chloride (284 µl, 3.0 M soln. in THF, 0.85 mmol, 5.0 eq) added dropwise causing the solution to become yellow. The reaction was refluxed for 1 h then cooled to ambient temperature and quenched with cold NH_4Cl (10 ml, sat. aq.). The solution was stirred for 15 min, then the phases were separated. The aqueous phase was re-extracted with ether (2x50 ml) and the combined organic extracts washed with water (30 ml), EDTA (30 ml, sat. aq./pH 3) and brine (30 ml), dried ($MgSO_4$), filtered and evaporated *in vacuo* to yield a yellow oil (168 mg). Purification by PLC (50% ether: petrol; SiO_2) gave **8** (18 mg, 40%) and **11** (12 mg, 30%).

Table 3, entry 2: To a solution of aziridine 4 (200 mg, 0.67 mmol) in THF (9.5 ml) was added dimethylsulfide (500 µl) and $CuBr.SMe_2$ (28 mg, 0.15 mmol, 0.2 eq).The resultant solution was cooled to -25°C and methyl magnesium chloride (1.13 ml, 3.0 M soln. in THF, 3.8 mmol, 5.0 eq) added dropwise. After 3 h at -25°C the reaction was quenched with cold NH_4Cl (10 ml, sat. aq.) and stirred for 15 min. Aqueous workup as above yielded a yellow oil (168 mg) which was purified by chromatography (gradient elution, 30-60% ethyl acetate: hexane; SiO_2) to give:

R_f (50% ethyl acetate: hexane) 0.35: (**8**) (92 mg, 50%).

R_f (50% ethyl acetate: hexane) 0.35: *(2R)-2-methyl-3-(N-para-toluenesulphonylamino)butan-2-ol* (**13**), colourless oil (54 mg, 30%): υ_{max} (neat) 3310(w) 2970(m) 1600(m) 1330(s) 1160(s) 1095(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.88 (3H, d, *J*=7.0 Hz, $CHC\underline{H}_3$), 1.05 (3H, s, $C\underline{H}_3$), 1.19 (3H, s, $C\underline{H}_3$), 1.47 (1H, bs, O<u>H</u>), 1.66-1.75 (1H, m, <u>H</u>-2), 2.43 (3H, s, $ArC\underline{H}_3$), 2.96 (2H, dt, *J*=2.0, 5.5 Hz, C(4)$\underline{H}_2$), 5.62 (1H, t, *J*=5.5 Hz, N<u>H</u>), 7.31 (2H, d, *J*=8.0 Hz, Ar C<u>H</u>), 7.76 (2H, d, *J*=8.5 Hz, Ar C<u>H</u>); δ_C (125 MHz, $CDCl_3$) 14.2 (C(2)$\underline{C}H_3$), 21.5 ($ArCH_3$), 24.8, 29.9 (C(1)($\underline{C}H_3$)$_2$), 42.4 (<u>C</u>-2), 46.1 (<u>C</u>-3), 74.2 (<u>C</u>-1), 127.1, 129.6 (Ar<u>C</u>H), 137.1, 143.1 (Ar *ipso*-<u>C</u>); m/e (NH_3 CI^+) 272 (MH^+, 20%), 259 (34%), 254 (70%), 242 (100%), 86 (40%).

Table 3, entry 3: To a solution of aziridine 4 (184 mg, 0.62 mmol) in THF (4.75 ml) was added dimethylsulfide (250 µl) and $CuBr.SMe_2$ (26 mg, 0.12 mmol, 0.2 eq). The resultant solution was cooled to -25°C and methyl magnesium chloride (1.04 ml, 3.0 M soln. in THF, 3.1 mmol, 5.0 eq) added dropwise. After 2 h at -25°C the reaction was quenched with cold NH_4Cl (10 ml, sat. aq.) and stirred for 15 min. Aqueous workup as above yielded a yellow oil (168 mg) which was purified by chromatography (50% ether: petrol; SiO_2) to give **9a** (19 mg, 10%), **10a** (78 mg, 40%) and **8** (59 mg, 35%).

Table 3, entry 5: To a solution of aziridine 4 (400 mg, 1.35 mmol) in THF (15 ml) was added dimethylsulfide (2 ml, co-solvent) and $CuBr.SMe_2$ (222 mg, 1.08 mmol, 0.8 eq). The resultant solution was cooled to -20°C and methyl magnesium chloride (896 µl, 3.0 M soln. in THF, 2.7 mmol, 2.0 eq) added dropwise. After 2 h at -20°C the reaction was quenched with cold NH_4Cl (10 ml, sat. aq.) and stirred for 1 h. Aqueous workup as above yielded a pale yellow oil (503 mg) which was purified by chromatography (gradient elution, 30-40% ethyl acetate: hexane; SiO_2) to give **9a** (127 mg, 30%) and **10a** (232 mg, 55%).

Table 3, entry 6: To a solution of aziridine 4 (96 mg, 0.32 mmol) in THF (4.75 ml) was added dimethylsulfide (250 µl) and $CuBr.SMe_2$ (13 mg, 0.06 mmol, 0.2 eq). The resultant solution was cooled to -78°C and n-Butyl magnesium chloride (808 µl, 2.0 M soln. in THF, 1.62 mmol, 5.0 eq) added dropwise. After 2 h at -78°C the solution was warmed to -25°C, stirred for 2 h and then quenched with cold NH_4Cl (10 ml, sat. aq.) and stirred for 15 min. Aqueous workup as above yielded a pale yellow oil. Purification by PLC (as entry 1) gave **9b** (34 mg, 30%), **10b** (34 mg, 30%) and **12** (38 mg, 40%).

Table 3, entry 7: To a solution of aziridine **4** (118 mg, 0.40 mmol) in THF (4.75 ml) was added dimethylsulfide (250 µl) and $CuBr.SMe_2$ (16 mg, 0.08 mmol, 0.2 eq). The resultant solution was cooled to -25°C and n-Butyl magnesium chloride (995 µl, 2.0 M soln. in THF, 2.0 mmol, 5.0 eq) added dropwise. After 2 h at -25°C the reaction was quenched with cold NH_4Cl (10 ml, sat. aq.) and stirred for 1 h. Aqueous workup as above yielded a brown oil (160 mg). Purification by PLC (as entry 1) gave **9b** (71 mg, 50%), **10b** (28 mg, 20%) and **12** (24 mg, 20%).

Table 3, entry 8: To a solution of aziridine **4** (70 mg, 0.24 mmol) in THF (4.75 ml) was added dimethylsulfide (250 µl) and $CuBr.SMe_2$ (16 mg, 0.08 mmol, 0.2 eq). The resultant solution was cooled to 0°C and n-Butyl magnesium chloride (590 µl, 2.0 M soln. in THF, 1.2 mmol, 5.0 eq) added dropwise. After 15 min at 0°C the reaction was quenched with cold NH_4Cl (10 ml, sat. aq.) and stirred for 1 h. Aqueous workup as above yielded a colourless oil (71 mg). Proton NMR (200 MHz) in dutero-chloroform revealed the crude product

to contain **9b**, **10b** and **12** in additiion to other products. Purification by PLC (as entry 1) gave **9b** (30 mg, 35%), **10b** (13 mg, 15%) and **12** (4 mg, 5%).

Table 3, entry 9: To a suspension of $CuBr.SMe_2$ (64 mg, 0.31 mmol, 0.2 eq) in 20% HMPA: THF (10 ml) at -12°C was added n-butyl magnesium chloride (3.87 ml, 2.0 M soln. in THF, 7.7 mmol, 5.0 eq). The resultant solution was stirred at this temperature for 15 min and then aziridine **4** (460 mg, 1.55 mmol) in 20% HMPA: THF (5 ml) added dropwise. After 1 h at -12°C the reaction was quenched with cold NH_4Cl (10 ml, sat. aq.) and stirred for 1 h. Aqueous workup as above yielded a yellow oil (540 mg) which was purified by chromatography (20% ether: petrol; SiO_2) to give **9b** (260 mg, 47%), **10b** (157 mg, 28%) and **12** (98 mg, 21%).

Table 3, entry 10: To a suspension of COD.CuCl (7 mg, $3.4x10^{-2}$ mmol, 0.2 eq) in 20% HMPA: THF (1 ml) at -10°C was added n-butyl magnesium chloride (446 µl, 2.0 M soln. in THF, 0.89 mmol, 5.0 eq). The resultant solution was stirred at this temperature for 15 min and then aziridine **4** (53 mg, 0.18 mmol) in 20% HMPA: THF (500 µl) added dropwise. After 1 h at -12°C the reaction was quenched with cold NH_4Cl (5 ml, sat. aq.) and stirred for 1 h. Aqueous workup as above yielded a yellow oil (58 mg). Purification by PLC (as entry 1) gave **9b**) (29 mg, 45%), **10b** (15 mg, 23%) and **12** (15 mg, 28%).

Table 3, entry 12: To a suspension of $CuBr.SMe_2$ (56 mg, 0.27 mmol, 0.2 eq) in 20% HMPA: THF (10 ml) at -16°C was added *iso*-propyl magnesium chloride (3.36 ml, 2.0 M soln. in THF, 6.7 mmol, 5.0 eq). The resultant solution was stirred at this temperature for 15 min and then aziridine **4** (400 mg, 1.35 mmol) in 20% HMPA: THF (5 ml) added dropwise. After 75 min at -16°C the reaction was quenched with cold NH_4Cl (10 ml, sat. aq.) and stirred for 1 h. Aqueous workup as above yielded a yellow oil (349 mg) which was purified by chromatography (gradient elution, 20-80% ether: petrol; SiO_2) to give:

R_f (50% ether: petrol) 0.75: *(2S)-(N-para-toluenesulphonylamino)-4-methylpentanoic acid tert-butyl ester* (**9c**) (182 mg, 40%), white crystalline solid: mp=94-96°C; $[\alpha]_D^{20}$ +18.9 (c. 0.83, CH_2Cl_2); υ_{max} ($CHCl_3$) 3340(w) 3023(m) 1730(s) 1345(m) 1165(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$); 0.92 (6H, d, *J*=6.5 Hz, $CH(C\underline{H}_3)_2$), 1.22 (9H, s, $C(C\underline{H}_3)_3$),1.44 (2H, t, *J*=7.0 Hz, β<u>H</u>'s), 1.85 (1H, septet, *J*=6.5 Hz, C(4)<u>H</u>), 2.40 (3H, s, $ArC\underline{H}_3$), 3.78 (1H, ddd, *J*=7.0, 10.0, 10.0 Hz, α<u>H</u>), 5.01 (1H, d, *J*=10.0 Hz, N<u>H</u>), 7.29 (2H, d, *J*=8.0 Hz, Ar<u>C</u>H), 7.73 (2H, d, *J*=8.5 Hz, Ar<u>C</u>H); δ_C (50 MHz, $CDCl_3$) 21.3 ($Ar\underline{C}H_3$), 22.7 ($CH(\underline{C}H_3)_2$), 24.2 (<u>C</u>-4), 27.5 ($C(\underline{C}H_3)_3$), 42.6 (β<u>C</u>), 54.8 (α<u>C</u>H), 82.2 ($\underline{C}(CH_3)_3$), 127.6, 129.8 (Ar<u>C</u>H), 137.0, 143.7 (Ar *ipso*-<u>C</u>), 171.8 ($\underline{C}O_2{}^tBu$); m/e (NH_3 DCI$^+$) 359 (MNH_4^+, 64%), 303 (MNH_5^+-^tBu, 100%), 286 (MH_2^+-^tBu, 18%), 240 (80%).

R_f (50% ether: petrol) 0.70: (**4**) (31 mg, 8%).

R_f (50% ether: petrol) 0.40: (**12**) (109 mg, 25%).

Table 3, entry 13: To a suspension of $CuBr.SMe_2$ (61 mg, 0.29 mmol, 0.2 eq) in 20% HMPA: THF (10 ml) at -16°C was added n-propyl magnesium chloride (3.70 ml, 2.0 M soln. in ether, 7.4 mmol, 5.0 eq). The resultant solution was stirred at this temperature for 15 min and then aziridine **4** (440 mg, 1.48 mmol) in 20% HMPA: THF (5 ml) added dropwise. After 75 min at -16°C the reaction was quenched with cold NH_4Cl (10 ml, sat. aq.) and stirred for 1 h. Aqueous workup as above yielded a yellow oil (451 mg) which was purified by chromatography (gradient elution, 20-80% ether: petrol; SiO_2) to give:

R_f (50% ether: petrol) 0.65: *(2S)-(N-para-toluenesulphonylamino)hexanoic acid tert-butyl ester* (**9d**) (210 mg, 42%), white crystalline solid: mp=97-98°C; $[\alpha]_D^{20}$ +21.2 (c. 0.91, CH_2Cl_2); Found C 59.5, H 8.2, N 4.0%, $C_{17}H_{27}NO_4S$ requires C 59.8, H 8.0, N 4.1%; υ_{max} ($CHCl_3$) 3340(w) 3023(m) 1730(s) 1345(m) 1165(s) cm^{-1}; δ_H (250 MHz, $CDCl_3$); 0.88 (3H, t, *J*=6.5 Hz, C(6)$\underline{H}_3$), 1.10-1.75 (6H, m, 3 x $C\underline{H}_2$), 1.26 (9H, s, $C(C\underline{H}_3)_3$), 2.40 (3H, s, $ArC\underline{H}_3$), 3.76 (1H, ddd, *J*=5.0, 7.5, 9.0 Hz, $\alpha\underline{H}$), 5.22 (1H, d, *J*=9.5 Hz, $N\underline{H}$), 7.28 (2H, d, *J*=8.0 Hz, Ar$\underline{CH}$), 7.73 (2H, d, *J*=8.5 Hz, Ar$\underline{CH}$); δ_C (125 MHz, $CDCl_3$) 13.6 ($\underline{C}$-6), 21.3 ($\underline{C}$-5), 21.9 ($Ar\underline{C}H_3$), 26.8 ($\underline{C}$-4), 27.5 ($C(\underline{C}H_3)_3$), 33.1 ($\underline{C}$-3), 56.1 ($\alpha\underline{C}H$), 82.2 ($\underline{C}(CH_3)_3$), 127.5, 129.7 (Ar$\underline{C}$H), 137.0, 143.6 (Ar *ipso*-$\underline{C}$), 171.2 ($\underline{C}O_2{}^tBu$); m/e (NH_3 DCI$^+$) 359 (MNH_4^+, 58%), 342 (MH^+, 5%) 303 (MNH_5^+-^{t}Bu, 100%), 286 (MH_2^+-^{t}Bu, 38%), 240 (50%).

R_f (50% ether: petrol) 0.55: *(2S)-(N-para-toluenesulphonylaminomethyl)pentanoic acid tert-butyl ester* (**10d**) (104 mg, 21%), colourless oil: υ_{max} ($CHCl_3$) 3340(w) 3020(m) 2960(m) 2940(m) 1715(s) 1335(m) 1160(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.87 (3H, t, *J*=7.0 Hz, C(5)$\underline{H}_3$), 1.20-1.60 (4H, m, 2 x CH_2), 1.42 (9H, s, $C(C\underline{H}_3)_3$), 2.43 (3H, s, $ArC\underline{H}_3$), 2.28-2.31 (1H, m, C(2)$\underline{H}$), 3.03 (2H, t, *J*=6.5 Hz, C(2)$C\underline{H}_2$), 5.02 (1H, t, *J*=6.5 Hz, $N\underline{H}$), 7.31 (2H, d, *J*=7.5 Hz, Ar$\underline{CH}$), 7.74 (2H, d, *J*=8.0 Hz, Ar$\underline{CH}$); δ_C (50 MHz, $CDCl_3$) 13.7 ($\underline{C}$-5), 19.9 ($\underline{C}H_2$), 21.4 ($Ar\underline{C}H_3$), 27.9 ($C(\underline{C}H_3)_3$), 31.6 ($\underline{C}H_2$), 43.7 (C(2)$\underline{C}H_2$), 45.2 ($\underline{C}$-2), 81.3 ($\underline{C}(CH_3)_3$), 127.1, 129.9 (Ar$\underline{C}$H), 137.1, 143.6 (Ar *ipso*-$\underline{C}$), 174.3 ($\underline{C}O_2{}^tBu$); m/e (NH_3 CI$^+$) 359 (MNH_4^+, 100%), 342 (MH^+, 12%) 303 (MNH_5^+-^{t}Bu, 17%), 286 (MH_2^+-^{t}Bu, 18%).

R_f (50% ether: petrol) 0.40: (**12**) (94 mg, 21%).

*Table 3, entry 14:*To a suspension of $CuBr.SMe_2$ (56 mg, 0.27 mmol, 0.2 eq) in 20% HMPA: THF (10 ml) at -20°C was added ethyl magnesium chloride (3.36 ml, 2.0 M soln. in ether, 6.7 mmol, 5.0 eq). The resultant solution was stirred at this temperature for 15 min and then aziridine **4** (400 mg, 1.35 mmol) in 20% HMPA: THF (4 ml) added dropwise. After 1 h at -20°C the reaction was quenched with cold NH_4Cl (10 ml, sat. aq.) and stirred for 1 h. Aqueous workup as above yielded a yellow oil (451 mg) which was purified by chromatography (gradient elution, 20-80% ether: petrol; SiO_2) to give:

R_f (50% ether: petrol) 0.65: *(2S)-(N-para-toluenesulphonylamino)pentanoic acid tert-butyl ester* (**9e**) (141 mg, 32%), white crystalline solid: mp=100-101°C; $[\alpha]_D^{20}$ +24.5 (c. 1.00, CH_2Cl_2); Found C 58.6, H 7.7, N 4.1%, $C_{16}H_{25}NO_4S$ requires C 58.7, H 7.7, N 4.3%; υ_{max} ($CHCl_3$) 3340(w) 3023(m) 1730(s) 1345(m) 1165(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$); 0.90 (3H, t, *J*=7.0 Hz, C(5)$\underline{H}_3$), 1.24 (9H, s, $C(C\underline{H}_3)_3$), 1.32-1.50 (2H, m, C(4)$\underline{H}_2$), 1.53-1.71 (2H, m, $\beta\underline{H}$'s), 2.40 (3H, s, $ArC\underline{H}_3$), 3.77 (1H, ddd, *J*=5.5, 7.5, 9.5 Hz, $\alpha\underline{H}$), 5.16 (1H, d, *J*=9.5 Hz, $N\underline{H}$), 7.28 (2H, d, *J*=8.0 Hz, Ar$\underline{CH}$), 7.73 (2H, d, *J*=8.5 Hz, Ar$\underline{CH}$); δ_C (50 MHz, $CDCl_3$) 13.3 ($\underline{C}$-5), 18.1 ($\underline{C}$-4), 21.3 ($Ar\underline{C}H_3$), 27.5 ($C(\underline{C}H_3)_3$), 35.5 ($\beta\underline{C}H_2$), 55.9 ($\alpha\underline{C}H$), 82.2 ($\underline{C}(CH_3)_3$), 127.4, 129.7 (Ar$\underline{C}$H), 137.0, 143.6 (Ar *ipso*-$\underline{C}$), 171.2 ($\underline{C}O_2{}^tBu$); m/e (NH_3 DCI$^+$) 345 (MNH_4^+, 100%), 289 (MNH_5^+-^{t}Bu, 22%), 272 (MH_2^+-^{t}Bu, 13%), 226 (36%).

R_f (50% ether: petrol) 0.55: *(2S)-(N-para-toluenesulphonylaminomethyl)butanoic acid tert-butyl ester* (**10e**) (86 mg, 20%), pale yellow oil: υ_{max} ($CHCl_3$) 3383(w) 3025(m) 2960(m) 2940(m) 1715(s) 1335(m) 1160(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.89 (3H, t, *J*=7.5 Hz, C(4)$\underline{H}_3$), 1.22 (9H, s, $C(C\underline{H}_3)_3$), 1.45-1.55 (2H, m, $\beta\underline{H}$'s), 2.42-2.44 (1H, m, $\alpha\underline{H}$), 2.42 (3H, s, $ArC\underline{H}_3$), 3.04 (2H, *ca.* t, *J*=6.5 Hz, C(2)$C\underline{H}_2$), 5.04 (1H, t, *J*=6.5 Hz, $N\underline{H}$), 7.31 (2H, d, *J*=7.5 Hz, Ar$\underline{CH}$), 7.77 (2H, d, *J*=8.0 Hz, Ar$\underline{CH}$); δ_C (50 MHz, $CDCl_3$) 11.1 ($\underline{C}$-4), 21.3 ($Ar\underline{C}H_3$), 22.7 ($\underline{C}$-3), 27.9 ($C(\underline{C}H_3)_3$), 43.4 (C(2)$\underline{C}H_2$), 46.9 ($\underline{C}$-2), 81.3 ($\underline{C}(CH_3)_3$), 127.4, 129.9 (Ar$\underline{C}$H), 140.6, 143.0 (Ar *ipso*-$\underline{C}$), 174.2 ($\underline{C}O_2{}^tBu$); m/e (NH_3 CI$^+$) 345 (MNH_4^+, 60%), 328 (MH^+, 12%) 289 (MNH_5^+-^{t}Bu, 100%), 272 (MH_2^+-^{t}Bu, 45%).

R_f (50% ether: petrol) 0.40: (**12**) (85 mg, 21%).

*Table 3, entry 15:*To a suspension of CuBr.SMe_2 (49 mg, 0.24 mmol, 0.2 eq) in 20% HMPA: THF (9 ml) at -16°C was added allyl magnesium chloride (2.94 ml, 2.0 M soln. in THF, 5.9 mmol, 5.0 eq). The resultant solution was stirred at this temperature for 15 min and then aziridine **4** (350 mg, 1.18 mmol) in 20% HMPA: THF (4 ml) added dropwise. After 80 min at -16°C the reaction was quenched with cold NH_4Cl (10 ml, sat. aq.) and stirred for 1 h. Aqueous workup as above yielded a yellow oil (422 mg) which was purified by chromatography (40% ether: petrol; SiO_2) to give:

R_f (50% ether: petrol) 0.70: (**4**) (105 mg, 30%).

R_f (50% ether: petrol) 0.50: *(2S)-N-para-toluenesulphonylaziridine-2-[1'-allyl-1'-hydroxybut-3'-ene* (**7f**) (145 mg, 40%), colourless oil: υ_{max} ($CHCl_3$) 3521(w) 3020(s) 2401(w) 1215(s) 1163(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.22-2.30 (4H, m, 2x$C\underline{H}_2CH{=}CH_2$), 2.38 (1H, d, *J*=4.5 Hz, <u>H</u>-3), 2.46 (3H, s, Ar$C\underline{H}_3$), 2.52 (1H, d, *J*=7.0 Hz, <u>H</u>-3), 2.93 (1H, dd, *J*=4.5, 7.0 Hz, <u>H</u>-2), 3.19 (1H, dd, *J*=6.5, 1.5 Hz, O<u>H</u>), 5.08-5.17 (4H, m, 2x$CH_2CH{=}C\underline{H}_2$), 5.72-5.93 (2H, m, $CH_2C\underline{H}{=}CH_2$), 7.36 (2H, d, *J*=8.0 Hz, Ar<u>C</u>H), 7.83 (2H, d, *J*=8.0 Hz, Ar<u>C</u>H); δ_C (125 MHz, $CDCl_3$) 21.6 (Ar$\underline{C}H_3$), 30.6 (<u>C</u>-3), 41.3, 44.2 ($\underline{C}H_2CH{=}CH_2$), 48.6 (<u>C</u>-2), 70.1 (<u>C</u>OH), 119.0, 119.7 ($CH_2CH{=}\underline{C}H_2$), 128.1, 129.7 (Ar<u>C</u>H), 132.2, 132.4 ($CH_2\underline{C}H{=}CH_2$), 134.8, 144.8 (Ar *ipso*-<u>C</u>); m/e (NH_3 CI^+) 308 (MH^+, 100%), 290 (20%), 266 (15%), 238 (10%), 152 (6%).

R_f (50% ether: petrol) 0.45: *N-para-toluenesulphonyl tert-butylamide* (27 mg, 10%), white crystalline solid: mp=107-108°C; δ_H (200 MHz, $CDCl_3$) 1.23 (9H, s, C($C\underline{H}_3$)$_3$), 2.43 (3H, s, Ar$C\underline{H}_3$), 4.60 (1H, bs, N<u>H</u>), 7.30 (2H, d, *J*=8.0 Hz, Ar<u>C</u>H), 7.79 (2H, d, *J*=8.0 Hz, Ar<u>C</u>H); m/e (NH_3 CI^+) 245 (MNH_4^+, 60%) 228 (MH^+, 80%), 212 (100%), 189 (95%), 155 (35%).

General procedure for the deprotection of N-para-toluenesulphonyl-amino acid tert-butyl ester derivatives to give amino acids:

A solution of HBr in acetic acid (3.0 ml, 33% w/v) was added dropwise to the diprotected amino acid (0.5 mmol) and phenol (1.0 mmol, 2.0 eq) and the solution stirred at ambient temperature for 24 h. After this time the reaction mixture was evaporated *in vacuo* , the residue dissolved in water (20 ml) and then extracted with ethyl acetate (20 ml). The phases were then separated and the aqueous phase was applied to a 'Dowex 50W-200' ion exchange column and eluted first with water (3x100 ml) and then ammonia (3x100 ml, 1.5 M aq.). Concentration of the first *ca.* 100 ml of ammonical eluant *in vacuo* followed by lyophilisation afforded the desired amino acid.

(2S)-Aminoheptanoic acid (**14b**):

9b (135 mg, 0.38 mmol) afforded **14b** as a white powder (28 mg, 51%): R_f (4: 1: 1: BuOH: AcOH: H_2O) 0.20; mp=274-276°C; $[\alpha]_D^{20}$ +22.6 (c. 0.45, HCl, 6.0 M aq.), [cf. Lit.[22(ii)] +23.9 (c. 0.04, HCl, 6.0 M aq.)]; υ_{max} (KBr) 2956(s) 1582(s) 1517(s) 1407(s) 849(w) cm^{-1}; δ_H (200 MHz, D_2O); 0.66 (3H, t, *J*=7.0 Hz, $C\underline{H}_3$), 1.18-1.21 (6H, m, 3x$C\underline{H}_2$), 1.55-1.70 (2H, m, β<u>H</u>'s), 3.53 (1H, t, *J*=6.0 Hz, α<u>H</u>); δ_C (125 MHz, D_2O); 13.9 ($\underline{C}H_3$), 22.3, 24.6, 31.1, 31.3 (4x$C\underline{H}_2$), 55.6 (α<u>C</u>H), 175.7 ($\underline{C}O_2^-$); m/e (NH_3 DCI^+) 146 (MH^+, 66%), 100 (100%).

(2S)-Amino-4-methyl-pentanoic acid (**14c**):

9c (91 mg, 0.27 mmol) afforded **14c** as a white powder (17 mg, 49%): mp=227-230°C (decomp.); $[\alpha]_D^{20}$ +21.0 (c. 0.32, HCl, 20% w/v aq.); υ_{max} (KBr) 2957(s) 2297(w) 1585(s) 1518(m) 1407(s) cm^{-1}; δ_H (300 MHz, D_2O); 0.79 (6H, dd, *J*=3.5, 6.0 Hz, CH($C\underline{H}_3$)$_2$), 1.49-1.61 (3H, m, C(4)<u>H</u>+β<u>H</u>'s), 3.57 (1H, t, *J*=5.5 Hz,

αH); δ_C (125 MHz, D_2O) 21.6, 22.7 ($CH(\underline{C}H_3)_2$), 24.9 (C-4), 40.5 (β$\underline{C}H_2$), 54.2 (α$\underline{C}$H), 176.2 ($\underline{C}O_2^-$); m/e (NH_3 DCI$^+$) 132 (MH^+, 100%), 86 (93%).

(2S)-Aminohexanoic acid (**14d**):

9d (120 mg, 0.35 mmol) afforded **14d** as a white powder (21 mg, 46%): R_f (4: 1: 1: BuOH: AcOH: H_2O) 0.50; mp=296-301°C; $[\alpha]_D^{20}$ +22.8 (c. 0.46, HCl, 6.0 M aq.), [cf. Lit.[22(iii)] +23.2 (HCl)]; υ_{max} (KBr) 2956(s) 2145(w) 1583(s) 1519(s) 1407(s) 865(w) cm^{-1}; δ_H (200 MHz, D_2O); 0.67 (3H, t, *J*=7.5 Hz, C$\underline{H}_3$), 1.05-1.15 (4H, m, 2xC$\underline{H}_2$), 1.57-1.68 (2H, m, β$\underline{H}$'s), 3.50 (1H, t, *J*=6.0 Hz, α$\underline{H}$); δ_C (125 MHz, D_2O); 13.6 ($\underline{C}H_3$), 22.3, 26.9 (2x$\underline{C}H_2$), 30.7 (β$\underline{C}H_2$), 55.6 (α$\underline{C}$H), 176.1 ($\underline{C}O_2^-$); m/e (Ar FAB$^+$) 132 (MH^+, 100%).

(2S)-Aminopentanoic acid (**14e**):

9e (103 mg, 0.31 mmol) afforded **14e** as a white powder (23 mg, 62%): R_f (4: 1: 1: BuOH: AcOH: H_2O) 0.50; mp=305-307°C; $[\alpha]_D^{20}$ +23.8 (c. 0.75, HCl, 20% w/v aq.), [cf. Lit.[22(iv)] +23.6 (c. 10, 20% HCl)]; υ_{max} (KBr) 2958(s) 2143(w) 1583(s) 1517(s) 1410(s) 851(w) cm^{-1}; δ_H (200 MHz, D_2O); 0.69 (3H, t, *J*=7.0 Hz, C$\underline{H}_3$), 1.13 (2H, sextet, *J*=8.0 Hz, C(4)$\underline{H}_2$), 1.52-1.63 (2H, m, β$\underline{H}$'s), 3.50 (1H, t, *J*=6.5 Hz, α$\underline{H}$); δ_C (125 MHz, D_2O); 13.5 ($\underline{C}H_3$), 18.4 (C-4), 30.7 (β$\underline{C}H_2$), 55.3 (α$\underline{C}$H), 176.1 ($\underline{C}O_2^-$); m/e (Ar FAB$^+$) 118 (MH^+, 100%).

(2R-Aminomethyl)propanoic acid (**15a**):

10a (206 mg, 0.64 mmol) afforded **15a** as a white powder (46 mg, 69%): mp=183-185°C; $[\alpha]_D^{20}$ -20.0 (c. 0.45, H_2O), [cf. Lit.[22(i)] -21 (c. 0.43, H_2O)]; υ_{max} (KBr) 3409(bs) 1627(s) 1571(s) 1468(s) 1412(s) 843(m) cm^{-1}; δ_H (200 MHz, D_2O); 0.96 (3H, d, *J*=7.5 Hz, C$\underline{H}_3$), 2.31-2.45 (1H, m, $\underline{H}$-2), 2.75-2.99 (2H, m, C(2)C$\underline{H}_2$); δ_C (50 MHz, D_2O); 15.6 ($\underline{C}H_3$), 39.7 (C-2), 42.9 (C(2)$\underline{C}H_2$), 182.3 ($\underline{C}O_2^-$); m/e (NH_3 CI$^+$) 104 (MH^+, 100%), 90 (20%).

(2S)-Aminopentanoic acid tert-butyl ester hydrochloride (**16**):

To a solution of (2S)-aminopentanoic acid (2.5 g, 21.4 mmol) in 1,4-dioxane (25 ml) and sulphuric acid (2.5 ml, conc., cat.) in a pressure flask was condensed isobutene (25 ml, excess.) and the flask sealed. The flask was shaken vigorously for 16 h afterwhich the excess isobutene was vented. The solution was poured onto a mixture of cold ether (200 ml) and sodium hydroxide (125 ml, 1.0 M aq). The ethereal phase was then separated off and the aqueous phase re-extracted with ether (2x100 ml). The combined ethereal extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo* until the total volume was *ca.* 30 ml. Dry HCl gas was then bubbled through the solution, precipitating the product as its hydrochloride salt (**16**) which was collected by suction filtration and recrystallised from dichloromethane-hexane as white crystals (1.28 g, 29%): mp=148-149°C; Found C 51.2, H 9.5, N 6.5%, $C_9ClH_{20}NO_2$ requires C 51.5, H 9.6, N 6.7%; υ_{max} ($CHCl_3$) 2980(s) 1740(s) 1520(s) 1371(s) 1156(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$).0.96 (3H, t, *J*=6.0 Hz, C$\underline{H}_3$), 1.50 (9H, s, C(C$\underline{H}_3$)$_3$), 1.48-1.59 (2H, m, C(4)$\underline{H}_2$), 1.92-2.06 (2H, m, β$\underline{H}$'s), 3.93 (1H, m, α$\underline{H}$), 8.76 (3H, bs, N$\underline{H}_3^+$); δ_C (50 MHz, $CDCl_3$) 13.4 (C-5), 18.1 (C-4), 27.8 (C($\underline{C}H_3$)$_3$), 32.5 (β$\underline{C}H_2$), 53.4 (α$\underline{C}$H), 83.8 ($\underline{C}$(CH$_3$)$_3$), 168.2 ($\underline{C}O_2$^{t}Bu); m/e (NH_3, DCI$^+$) 174 ($C_9H_{20}NO_2^+$, 42%), 118 (100%), 72 (85%).

N-para-Toluenesulphonyl-(2S)-aminopentanoic acid tert-butyl ester (**9e**):

To a solution of **16** (40 mg, 1.9 mmol) in dichloromethane (5 ml) under argon at 0°C was added triethylamine (534 μl, 3.8 mmol, 2.0 eq) and *para*-toluenesulphonyl chloride (365 mg, 1.9 mmol, 1.0 eq) in

dichloromethane (3 ml) dropwise. The solution was stirred for 3 h at ambient temperature and then filtered to remove the precipitate (triethylamine hydrochloride) and the filtrate concentrated *in vacuo*. The residue was re-dissolved in ethyl acetate (20 ml), washed with citric acid (20 ml, 1.0 M aq.), $NaHCO_3$ (20 ml, 1.0 M aq.) and water (20 ml) dried (Na_2SO_4), filtered and concentrated *in vacuo* to yield a white solid (515 mg) which was purified by chromatography (30% ether: petrol; SiO_2) to give **9e** (401 mg, 82%): $[\alpha]_D^{20}$ +24.4° (c. 1.00, CH_2Cl_2) [cf. $[\alpha]_D^{20}$ +24.5° (c. 1.00, CH_2Cl_2) for ring opened material].

(±)-2,3-Dibromopropionic acid tert-butyl ester (±**18**):

To a solution of *tert*-butyl acrylate (72.60 ml, 0.50 M) in anhydrous carbon tetrachloride (100 ml), cooled to 0°C, was added dropwise neat dibromine (25.70 ml, 0.50 M, 1.0 eq), ensuring that the temperature at no time during the addition exceeded 10°C. After a further 1 h the solvent was removed *in vacuo* to yield ±**18** (143 g, 100%): R_f (50% ether: petrol) 0.90; Found C 29.2, H 4.2%, $Br_2C_7H_{12}O_2$ requires C 29.2, H 4.2%; υ_{max} (neat) 2981(m) 2935(w) 1741(s) 1371(s) 1253(s) 1144(s) 841(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.40 (9H, s, $C(C\underline{H}_3)_3$), 3.55 (1H, dd, *J*=4.5, 9.5 Hz, <u>H</u>-2), 3.76 (1H, dd, *J*=9.5, 11.0 Hz, <u>H</u>-3), 4.24 (1H, dd, *J*=4.5, 11.0 Hz, <u>H</u>-3), δ_C (50 MHz, $CDCl_3$) 27.5 ($C(\underline{C}H_3)_3$), 29.9 (<u>C</u>-3), 42.6 (<u>C</u>-2), 83.3 ($\underline{C}(CH_3)_3$), 166.5 ($\underline{C}O_2{}^tBu$); m/e (NH_3 CI^+) 308 (60%), 306 (MNH_4^+, 100%), 304 (70%), 74 (15%).

(±)-Aziridine-2-carboxylic acid tert-butyl ester (±**19**):

Ammonia (600 ml, excess.) was condensed under argon into a flame dried three necked 1 l round bottom flask equipped with an efficient magnetic stirrer. The dibromide (±**18**) (40.0 g, 139 mmol) was added dropwise over 1 h and the solution stirred vigorously for a further 2 h prior to evaporation of the excess ammonia. The resultant white residue was partitioned between ether (250 ml) and brine (100 ml), the phases separated and the aqueous phase re-extracted with ether (2x100 ml). The combined ethereal layers were dried ($MgSO_4$), filtered and evaporated *in vacuo* to yield a pale yellow oil which was purified by rapid vacuum distillation employing a 'dry ice trap' (43°C, 3 mmHg) to yield the desired product (±**19**) as a colourless oil (15.2 g, 76%): R_f (50% ether: petrol) 0.30; Found C 58.5, H 9.2, N 9.7%, $C_7H_{13}NO_2$ requires C 58.7, H 9.2, N 9.8%; υ_{max} (neat) 3288(w) 2981(m) 2936(w) 1723(s) 1396(s) 1370(s) 1241(s) 1162(s) 824(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.91 (1H, bs, N<u>H</u>), 1.44 (9H, s, $C(C\underline{H}_3)_3$), 1.74 (1H, dd, *J*=1.0, 5.5 Hz, <u>H</u>-3), 1.87 (1H, dd, *J*=1.5, 3.0 Hz, <u>H</u>-3), 2.37 (1H, dd, *J*=3.0, 5.5 Hz, <u>H</u>-2); δ_C (125 MHz, $CDCl_3$) 25.8 (<u>C</u>-3), 27.1 ($C(\underline{C}H_3)_3$), 28.7 (<u>C</u>-2), 80.7 ($\underline{C}(CH_3)_3$), 171.1 ($\underline{C}O_2{}^tBu$); m/e (NH_3 CI^+) 144 (MH^+, 100%), 88 (85%).

(±)-N-Methanesulphonylaziridine-2-carboxylic acid tert-butyl ester (±**20a**):

To a solution of aziridine ±**19** (1.50 g, 10.5 mmol) in dichloromethane (15 ml) under argon at 0°C was added triethylamine (1.61 ml, 11.5 mmol, 1.1 eq) and methanesulphonyl chloride (898 µl, 11.5 mmol, 1.1 eq) dropwise. A white precipitate (triethylamine hydrochloride) was deposited and after stirring for a further 1 h at 0°C the solution was filtered through a plug of Celite®, concentrated *in vacuo* and purified by chromatography (30% ethyl acetate: hexane; SiO_2) to yield ±**20a** as a white crystalline solid (2.22 g, 96%): R_f (50% ethyl acetate: hexane) 0.55; mp=55-56°C; Found C 43.4, H 6.9, N 6.5, S 14.5%, $C_8H_{15}NO_4S$ requires C 43.4, H 6.8, N 6.3, S 14.5%; υ_{max} (neat) 2937(m) 1741(s) 1397(s) 1163(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.41 (9H, s, $C(C\underline{H}_3)_3$), 2.47 (1H, d, *J*=4.0 Hz, <u>H</u>-3), 2.60 (1H, d, *J*=7.0 Hz, <u>H</u>-3), 3.05 (3H, s, $SO_2C\underline{H}_3$), 3.10 (1H, dd, *J*=4.0, 7.0 Hz, <u>H</u>-2); δ_C (50 MHz, $CDCl_3$) 27.6 ($C(\underline{C}H_3)_3$), 31.3 (<u>C</u>-3), 35.9 (<u>C</u>-2), 39.4 ($SO_2\underline{C}H_3$), 83.1

165.9 ($\underline{C}O_2{}^tBu$); m/e (NH_3 CI^+) 239 (MNH_4^+, 51%), 222 (MH^+, 4%), 183 (MNH_5^+-^{t}Bu, 100%), $_2^+$-^{t}Bu, 90%).

(±)-N-iso-Propylsulphonylaziridine-2-carboxylic acid tert-butyl ester (**±20b**):

To a solution of the aziridine (**±19**) (1.50 g, 10.5 mmol) in dichloromethane (50 ml) under argon at 0°C was added triethylamine (2.92 ml, 21 mmol, 2.0 eq) and *iso*-propylsulphonyl chloride (2.35 ml, 21 mmol, 2.0 eq) dropwise. A white precipitate (triethylamine hydrochloride) was deposited and after stirring for a further 3 h at ambient temperature the solution was filtered, the filtrate concentrated *in vacuo* and the residue dissolved in ethyl acetate (20 ml), washed with brine (3x20 ml), dried ($MgSO_4$), re-filtered and *in vacuo* evaporated *in vacuo* to yield a thick yellow oil (2.9 g). Purification by chromatography (30% ether: petrol; SiO_2) yielded crude **±20b** as a yellow oil which was purified further by bulb to bulb distillation (190°C, 2 mmHg) (1.27 g, 49%): R_f (50% ether: petrol) 0.48; Found C 47.9, H 7.8, N 5.6, S 12.6%, $C_{10}H_{19}NO_4S$ requires C 48.2, H 7.7, N 5.6, S 12.9%; υ_{max} (neat) 2982(w) 1743(s) 1326(s) 1239(s) 1149(s) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.45 (6H, d, *J*=7.0 Hz, $CH(C\underline{H}_3)_2$), 1.46 (9H, s, $C(C\underline{H}_3)_3$), 2.50 (1H, d, *J*=4.0 Hz, $\underline{H}_c$-3), 2.66 (1H, d, *J*=7.0 Hz, $\underline{H}_b$-3), 3.14 (1H, dd, *J*=4.0, 7.0 Hz, $\underline{H}_a$-2), 3.36 (1H, septet, *J*=7.0 Hz, $C\underline{H}(CH_3)_2$); δ_C (50 MHz, $CDCl_3$) 16.0 ($CH(\underline{C}H_3)_2$), 27.7 ($C(\underline{C}H_3)_3$), 30.5 ($\underline{C}$-3), 36.4 ($\underline{C}$-2), 53.9 ($\underline{C}H(CH_3)_2$), 83.0 ($\underline{C}(CH_3)_3$), 166.2 ($\underline{C}O_2{}^tBu$); m/e (NH_3 CI^+) 267 (MNH_4^+, 32%), 250 (MH^+, 8%), 211 (MNH_5^+-^{t}Bu, 100%), 194 (MH_2^+-^{t}Bu, 41%).

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