Pergamon

Tetrahedron, Vol. 52, No. 40, pp. 13035-13050, 1996

0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00784-3

Regioselective Nucleophilic Ring Opening Reactions of 2,2-Disubstituted Aziridines - the Asymmetric Synthesis of α,α-Disubstituted Amino Acids

Beatrice G. M. Burgaud, David C. Horwell, Allessandro Padova and Martyn C. Pritchard.*

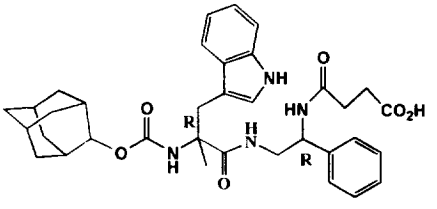
Parke-Davis Neuroscience Research Centre, Cambridge University Forvie Site, Robinson Way, CAMBRIDGE, CB2 2QB, UK.

Abstract : In this paper a broadly applicable synthesis of chiral α,α-disubstituted amino acids is outlined based upon regioselective ring opening of aziridine derivatives. Examples of nitrogen, sulphur and carbon nucleophiles were found to preferentially attack the C3 position of chiral 2-methyl-2-silyloxymethyl aziridines to provide a range of α,α-disubstituted amino acid derivatives in good yield.

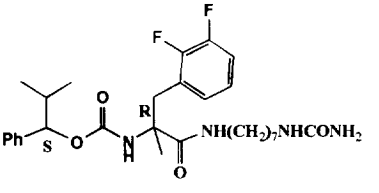
INTRODUCTION

We have previously published the preparation[1] and application[2] of α,α-disubstituted amino acids in the design and synthesis of high affinity ligands for cholecystokinin (CCK) and tachykinin (NK) receptors (see figure 1 for examples of CCK-B[3] and NK_3[4] receptor ligands containing α-methyl amino acid residues). Extensive use of this class of molecule has been made by us since in addition to exhibiting enhanced chemical and *in vivo* stability when compared to its corresponding α-amino acid parent,[5] these mono amino acids have the potential to stabilise preferred biologically active conformations due to the restricted rotation imparted by the additional α-substituent.[6]

By far the majority of published syntheses of both racemic and chiral α,α-disubstituted amino acids have involved the alkylation of suitably derivatised α-amino acids via the intermediacy of a stabilised carbanion.[7] A requirement for this approach is the availability of suitably protected electrophiles. In order to increase the diversity of α,α-disubstituted amino acid targets available, we wished to devise a broadly applicable synthesis of α,α-disubstituted amino acids which involved a complementary nucleophilic substitution strategy. One method of achieving this objective would be an S_N2-mediated ring opening reaction on aziridine 2-methyl-2-carboxylate esters induced by nucleophilic attack at C3 (scheme 1).

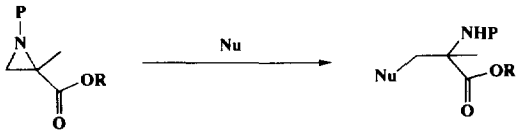


CI-988
CCK-B Receptor Ligand



PD 161182
NK_3 Receptor Ligand

Figure 1



Scheme 1

There have been a number of publications demonstrating the utility of aziridine-2-carboxylates in the preparation of α- and β-amino acids.[8] The first examples, to our knowledge, of the synthesis of α,α-disubstituted amino acids using this approach have been described in recent publications from Wipf et al.[9] and Goodman et al.[10] which outline the synthesis of α-methyl serine and cysteine derivatives respectively.

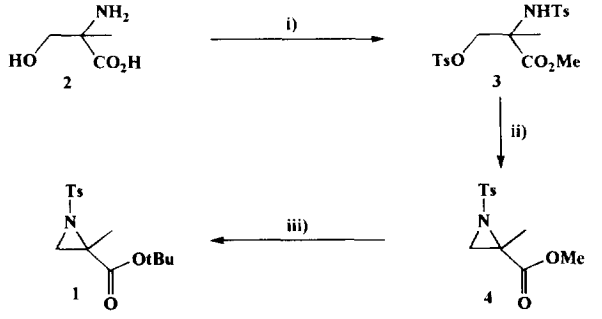
In this paper we will describe the outcome of the reactions of a variety of carbon and heteroatom-based nucleophiles on aziridine-2-methyl-2-carboxylate derivatives. We believe this methodolgy will prove broadly applicable to the efficient chiral synthesis of α,α-disubstituted amino acids.

RESULTS AND DISCUSSION

Nucleophilic Ring Opening Reactions of Racemic 2-Methyl-2-Carboxylate Substituted Aziridine

In the first series of reactions attempted, we explored the regioselectivity of reaction of a diverse set of nucleophiles with the racemic aziridine-2-methyl-2-carboxylate derivative (**1**). The carboxylic acid group on the aziridine (**1**) was derivatised as a sterically demanding *t*-butyl ester[11] in order to promote C3 attack whilst the nitrogen atom was protected by a tosyl moiety. Although potentially more difficult to remove than acyl or alkoxycarbonyl alternatives, a sulphonyl group was selected for protection of the nitrogen atom in **1** since its stronger electron withdrawing capability should hasten what is a potentially slow nucleophilic substitution onto a neopentyl C3 position.[12]

The synthesis of the target aziridine derivative (**1**) is outlined in scheme 2 and involves, initially, esterification and tosylation of the commercially available (RS)-α-methyl serine (**2**) followed by base catalysed cyclisation to provide the aziridine (**4**). Subsequent saponification of the methyl ester followed by conversion of the resulting carboxylic acid to its *t*-butyl ester[13] yielded the target aziridine substrate **1**.

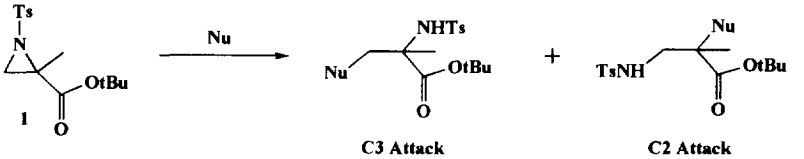


Scheme 2

Reagents and conditions : i) a)HCl,MeOH; b)TsCl,Pyridine; ii)TEA,THF; iii) a)LiOH Dioxane/Water; b)$Cl_3CC(=NH)OtBu$,THF,cyclohexane,$BF_3.Et_2O$.

In selecting a diverse range of nucleophiles to investigate, examples of hard (eg. HCl, HCOOH), borderline (eg. NaN_3, $PhCH_2NH_2$) and soft (eg. PhSH, cuprates) nucleophiles (as characterised by the semi-empirical molecular orbital programme MOPAC[14]) have been included. The outcome of the effect of these various nucleophiles on reaction with the aziridine **1** is summarised in table 1.

Table 1 : Reaction of Selected Nucleophiles with Aziridine-2-Methyl-2-*t*-Butyl Carboxylate 1



C3 Attack C2 Attack

Entry	Reagent	Conditions	Ratio C3/C2Attack	Overall Yield
1	**HCl**	Et_2O, 72h, 20°C	1 / 4	87%
2	**HCOOH**	1h, 0°C	1 / 1	95%
3	**$PhCH_2NH_2$**	THF, 16h, reflux	C3 attack only	84%
4	**NaN_3**	DMF, 72h, 20°C	1 / 4	75%
5	**PhSH**	DMF, 72h, 20°C	1 / 1	85%
6	**iPrMgCl/CuBr.SMe_2**	THF,1h,reflux	C3 attack only	60%
7	**PhMgBr/CuBr.SMe_2**	THF,1h,reflux	C3 attack only	52%
8	**Indole/MeMgBr/ CuBr.SMe_2**	THF,16h,reflux	C3 attack only	48%

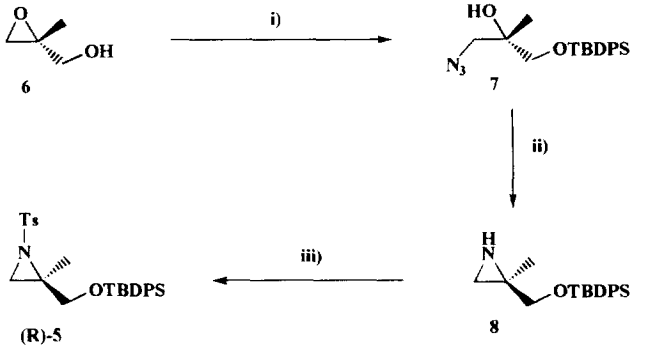
Most encouraging amongst these reactions was the excellent regioselectivity achieved by the aziridine ring opening with organocuprates. In the three examples listed in table 1, cuprate reagents were found to open the aziridine **1** at C3 with complete regioselectivity to provide the required α-amino acid in good to moderate yields giving no quantifiable levels of the corresponding β-amino acid as shown by the absence or presence of $NHCH_2$ coupling in ^{1}HNMR spectra.[15] These findings are in marked contrast to the reactions of organocuprate reagents with corresponding des-methyl aziridine-2-carboxylate esters which were found to yield mixtures of α- and β-amino acids in addition to products arising from reduction.[13] Regioselectivity can be achieved for such reactions on des-methyl aziridine-2-carboxylates, however, if the ester is replaced by a free carboxylic acid[16] or the tosyl moiety is changed to a *t*-butyloxycarbonyl urethane N-protecting group.[13a] Among the various nucleophiles explored the only other regioselective reaction occurred on reaction of the borderline hard/soft nucleopile benzylamine (see table 1). As with the soft organocuprate nucleophiles, benzylamine attacks exclusively the C3 position. Mixtures of α- and β-amino acids were isolated when the aziridine **1** was reacted with hard nucleophiles (HCl, HCOOH), the borderline nucleophile NaN_3 and the soft nucleophile PhSH. The attack at both C2 and C3 positions occuring on reaction with HCl and NaN_3 is consistent with results obtained on reaction of the same reagents on des-methyl aziridine-2-carboxylate esters.[17] However, thiols and carboxylic acids regioselectively open des-methyl aziridine-2-carboxylate esters at the C3 position which is, as was the case with reaction with organocuprates, in contrast to our findings with 2,2-disubstituted aziridines.[17]

Although it would be inappropriate, given the limited number of examples, to derive from these data any firm rules to predict the outcome of aziridine ring opening, one may generalise that C3 attack on this particular class of aziridine is most likely to occur with soft nucleophiles.

Nucleophilic Ring Opening Reactions of Chiral 2-Methyl-2-Silyloxymethyl Substituted Aziridines

Having established the regioselectivity of a variety of nucleophiles with the racemic aziridine **1**, we subsequently turned our attention toward realising the potential of the chiral synthesis of α-amino acids via this approach. The key aziridine substrate selected for this study was the silyl ether **5** and not the corresponding chiral version of the racemic aziridine **1**. The reduced derivative **5** was preferred over **1** since it was envisaged that the bulky silyl group would, like the t-butyl moiety, be sufficiently sterically demanding to promote C3 attack and this effect, we hypothesised, would also be attenuated by removal of the electron withdrawing carboxyl group. It was hoped that these changes to the aziridine substrate would encourage preferential attack at the C3 position for all types of nucleophile.

The synthesis of the target aziridine (R)-**5** is outlined in scheme 3 and is similar in approach to previous chiral syntheses of aziridines published by Zwanenburg,[17] Wipf[9] and Goodman.[10] Yields quoted in the scheme represent those achieved in the process of preparing (R)-**5** although, as one might expect, similar yields were obtained in the synthesis of the corresponding R antipode. Beginning with the commercially available (R)-2-methylglycidol (**6**), protection of the alcohol as its silyl ether followed by regioselective ring opening with NaN_3[9,10] provided the azido alcohol **7** in excellent yield. A subsequent Staudinger reaction was carried out on the azido alcohol intermediate **7** and the resulting aziridine N-protected with a tosyl moiety to give the required chiral aziridine substrate (R)-**5**.



Scheme 3

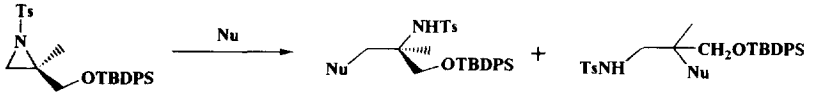
Reagents and conditions : i)a)TBDPSCl,imidazole,DMAP,DCM; b)NaN_3,MeOH,H_2O; ii)Ph_3P,THF; iii)TsCl,TEA,THF

Following completion of the synthesis of the chiral aziridine substrates (R)-**5** and (S)-**5**, both compounds were then reacted with the same diverse set of nucleophiles, with the addition of benzyl alcohol, under conditions previously selected for reaction with the racemic aziridine **1** (tables 2 and 3).

As was found with the racemic aziridine-2-methyl-2-carboxylate (**1**), regioselective attack on the C3 position was achieved on reaction of organocuprates with the chiral 2-methyl-2-silyloxymethyl substituted aziridines (R)-**5** and (S)-**5** (see tables 2 and 3). Even more encouraging, however, was the regioselectivity obtained on reaction of NaN_3 and PhSH with the chiral aziridines. In contrast to the corresponding reactions with the racemic aziridine carboxylate (**1**) (see table1), both the nucleophiles generated from the reagents NaN_3 and PhSH attacked solely, within the limits of ^{1}HNMR detection, the C3 position of the chiral aziridines

(R)-5 and (S)-5. These latter findings help to substantiate the hypothesis that the electron withdrawing carboxyl group in the racemic aziridine 1 was actively promoting attack at the C2 position. Only the hard nucleophiles arising from the reagents HCl, HCOOH and $PhCH_2OH/BF_3.Et_2O$ ($PhCH_2OH$ did not react in the absence of acid) failed to open the chiral aziridine substrates in the desired manner yielding a mixture of α- and β-amino acids in the HCl reaction and a β-amino acid upon reaction of the aziridines with HCOOH and $PhCH_2OH$. These latter exceptions to regioselective C3 attack may not solely be due to the hardness of the nucleophiles employed but may also be a function of the acidic reaction conditions which may promote attack at the more hindered C2 carbon atom.[8]

Table 2 :Reaction of Selected Nucleophiles with 2-Methyl-2-Silyloxymethyl Substituted Aziridine (R)-5



(R)-5

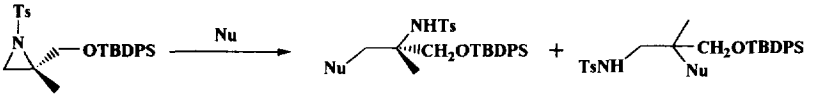
		C3 Attack		C2 Attack	
Entry	**Reagent**	**Conditions**	**Ratio C3/C2Attack**	**$[\alpha]_D$ CH_2Cl_2[a]**	**Overall Yield**
1	**HCl**	Et_2O, 72h, 20°C	1 / 1.25	-1.2/+8.3	95%
2	**HCOOH**	1h, 0°C	C2 attack only	-6.9	78%
3	**$PhCH_2OH$**	CH_2Cl_2, $BF_3.Et_2O$ 16h, 20°C	C2 attack only	+7.9	67%
4	**$PhCH_2NH_2$**	THF, 16h, reflux	C3 attack only	-1.0	96%
5	**NaN_3**	DMF, 72h, 20°C	C3 attack only	-13.9	90%
6	**PhSH**	DMF, 72h, 20°C	C3 attack only	-12.9	90%
7	**iPrMgCl/CuBr.SMe_2**	THF,1h,reflux	C3 attack only	+5.0	78%
8	**PhMgBr/CuBr.SMe_2**	THF,1h,reflux	C3 attack only	+9.6	75%
9	**Indole/MeMgBr/ CuBr.SMe_2**	THF,16h,reflux	C3 attack only	+3.8	71%

a) Where two rotations are quoted the first value relates to the optical activity of the α-amino acid whereas the latter refers to that of the corresponding β-amino acid

Products arising from ring opening of the S-configured aziridine (S)-5 exhibited equal and opposite optical rotation values to the equivalent products derived from the corresponding R antipode, (R)-5. Although this finding would clearly be expected for the α-amino acids that were prepared, equal and opposite rotations were also recorded for the β-amino acids arising from reaction of the chiral aziridine substrates with HCl, HCOOH and $PhCH_2OH/ BF_3.Et_2O$. This latter result would suggest, although not definitively prove, that attack at the C2 position also proceeds via an S_N2 reaction mechanism under the conditions studied.

Despite the failure of hard nucleophiles to regioselectively open the chiral aziridines at the C3 position, tables 2 and 3 list examples of nitrogen, sulphur and carbon nucleophiles which regioselectively open chiral aziridine substrates to provide derivatives of chiral α,α-disubstituted amino acids in good chemical yield.

Table 3 :Reaction of Selected Nucleophiles with 2-Methyl-2-Silyloxymethyl Substituted Aziridine (S)-5



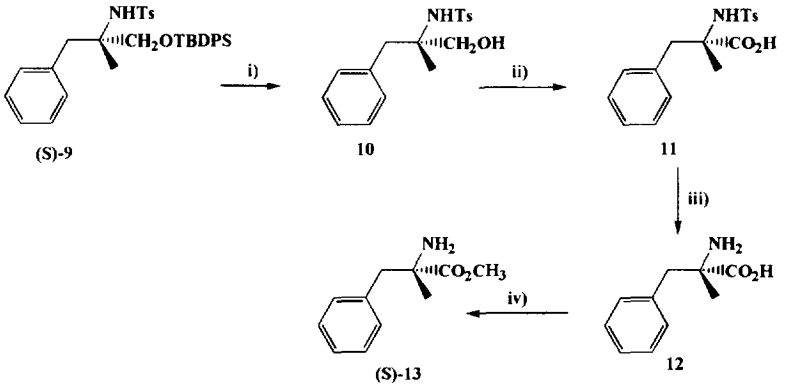
(S)-5

			C3 Attack	C2 Attack	
Entry	**Reagent**	**Conditions**	**Ratio C3/C2Attack**	**$[\alpha]_D$ CH_2Cl_2[a]**	**Overall Yield**
1	**HCl**	Et_2O, 72h, 20°C	1 / 1.25	+1.6/-8.9	92%
2	**HCOOH**	1h, 0°C	C2 attack only	+4.5	87%
3	**$PhCH_2OH$**	CH_2Cl_2, $BF_3.Et_2O$ 16h, 20°C	C2 attack only	-8.4	63%
4	**$PhCH_2NH_2$**	THF, 16h, reflux	C3 attack only	+1.0	93%
5	**NaN_3**	DMF, 16h, 20°C	C3 attack only	+14.6	87%
6	**PhSH**	DMF, 16h, 20°C	C3 attack only	+13.3	84%
7	**$iPrMgCl/CuBr.SMe_2$**	THF,1h,reflux	C3 attack only	-5.7	71%
8	**$PhMgBr/CuBr.SMe_2$**	THF,1h,reflux	C3 attack only	-10.7	77%
9	**Indole/MeMgBr/ $CuBr.SMe_2$**	THF,16h,reflux	C3 attack only	-4.2	67%

a) Where two rotations are quoted the first value relates to the optical activity of the α-amino acid whereas the latter refers to that of the corresponding β-amino acid

Preparation of α,α-Disubstituted Amino Acids

In order to demonstrate that α,α-disubstituted amino acids could directly be derived by applying this methodology, **(S)-9** (entry 8, table 3) was converted to the methyl ester of (S) α-methyl phenyl alanine **(13)** (scheme 4). Initial removal of the silyl protecting group followed by oxidation of the newly exposed hydroxyl function provided the N-tosyl amino acid **11**. Acidic mediated cleavage of the N-tosyl moiety and subsequent methanolysis of the intermediate amino acid **12** provided (S) α-methyl phenyl alanine **(13)** with an optical rotation identical to that previously reported in the literature.[18]



Scheme 4

Reagents and conditions i) TBAF, THF; ii)$K_2Cr_2O_7$, H_2SO_4, H_2O, 0°C to RT; iii)32%HBr/HOAc; iv)$SOCl_2$, MeOH,reflux.

CONCLUSIONS

In this study we have demonstrated that, under appropriate conditions, 2,2-disubstituted aziridines undergo regioselective ring opening reactions at the C3 position with nitrogen, sulphur and carbon nucleophiles to provide chiral α,α-disubstituted amino acid derivatives in good chemical yield. We believe this methodology will prove to be a generally applicable synthesis of chiral α,α- disubstituted amino acids and will be complementary to existing carbanion-based approaches to the preparation of this important class of unnatural α-amino acids.

EXPERIMENTAL

General procedures. Commercially available solvents and reagents were used throughout without further purification, dry solvents (over molecular sieves) were used where appropriate. Solvent evaporation was carried out using a Büchi R110 or R134 rotary evaporator. Reactions were performed under an inert atmosphere of argon or nitrogen where appropriate. Analytical TLC (Thin layer Chromatography) was performed on silica gel 60_{254} plates, (Merck Art 5719), and $KC_{18}F$ (octadecylsilane bonded) reverse phase plates (Whatman 4803 600). The chromatograms were viewed under U.V. light at 254 nm and/or developed with iodine vapour. Normal phase chromatography refers to the flash method and was performed on Kieselgel 60 (230-400 mesh) silica. Medium pressure reverse phase chromatography was performed on a Gilson apparatus using Lichromprep® RP-18 (230-400 mesh silica). HPLC was performed on a Beckman System Gold reverse phase high performance liquid chromatography system using a Lichrosorb® RP-18 column. All silica was supplied by E. Merck, A. G., Darmstardt, Germany. Melting points were determined with a Mettler FP800 or a Reichert Thermometer hot stage apparatus. Optical rotations ([ ]$_D$) were measured employing the solvents and temperatures specified using a Perkin-Elmer 241 polarimeter. Elemental analysis was performed by Medac Ltd, Dept. of Chemistry, Brunel University, Uxbridge, Middlesex or by Butterworth Laboratories Ltd.,Teddington, Middlesex. I.R. spectra were recorded on either a Perkin Elmer 1750 or 2000 Fourier transform I.R. spectrometer, the samples being analyzed as thin films on a sodium chloride disc or as a potassium bromide disc. ^{1}H-NMR spectra were recorded on either a Bruker AM 300 spectrometer (300 MHz) or a Varian Unity Plus 400 (400 MHz). Chemical shifts are reported in parts per million downfield from tetramethylsilane ($SiMe_4$) by reference to the residual protons of the respective solvents. Coupling constants (*J*) in Hertz are included where possible. ^{13}C-NMR Spectra were recorded on a Varian Unity Plus 400 (100 MHz). Fast atom bombardment (FAB), electron ionization (EI), chemical ionisation (CI) and atmospheric pressure chemical ionization (APCI) mass spectra were performed either on a Finnegan 4500 spectrometer at Parke-Davis, Ann Arbor, Michigan, United States; or by the SERC Mass Spectrometry Service Centre, University of Wales, Swansea, on a VG Mass Lab model 12/253 or a VG Analytical model ZAB/E.

Experimental procedures :

2-Methyl-2-(toluene-4-sulphonylamino)-3-(toluene-4-sulphonyloxy)-propionic acid methyl ester 3 : HCl gas was bubbled through a cooled solution (0 C) of (R,S)-α-methyl serine **2** (2.00 g, 16.80 mmol) in methanol (350 cm^3) until saturation. The solution was heated under reflux for 4 h and the solvent evaporated *in vacuo* to yield a thick colourless oil. To this solution of serine methyl ester in pyridine (50 cm^3) at 0 C was added dropwise a solution of *p*-toluenesulphonyl chloride (12.77 g, 67.22 mmol) in pyridine (20 cm^3), ensuring that the temperature of the solution was maintained below 0 C. The solution was stirred at 0 C for 5 h. The resulting solution was allowed to warm to room temperature and stirred for 16 h. The pyridine was removed *in vacuo* and the residual brown paste dissolved in ethyl acetate (400 cm^3). The solution was washed with copper sulphate (10% w/v aq.) (200 cm^3), citric acid (10% w/v aq.) (200 cm^3) and water (200 cm^3). The organic phase was dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo*. Recrystallisation from diethyl ether yielded **3** as a white solid. (3.94 g, 81%), mp 153-155 C (from diethyl ether); (found: C, 51.60; H, 5.30; N, 3.22; S, 14.35. $C_{19}H_{23}NO_7S_2$ requires C, 51.69; H, 5.25; N, 3.17; S, 14.52%); $_{max}$ (film)/cm^{-1} 3322 (NH), 2954 (CH), 1736 (C=O), 1361 and 1177 (SO_2); $_H$(400MHz, $CDCl_3$) 1.40 (3H, s, CH_3), 2.41 (3H, s, $C_4H_6C\underline{H}_3$), 2.45 (3H, s, $C_4H_6C\underline{H}_3$), 3.67 (3H, s, CO_2CH_3), 4.22(2H,s,CH_2),5.47 (1H, s, $N\underline{H}SO_2C_6H_4$), 7.26 (2H, d, *J* 8, Ar-H),

7.35 (2H, d, *J* 8, Ar-H) and 7.71 (4H, t, *J* 8, Ar-H); *m/z* (APCI) 422 (M+H, 100%) and 270 (90); (found 442.099212. $C_{19}H_{24}NO_7S_2$ requires 442.099421).

***2-Methyl-1-(toluene-4-sulphonyl)-aziridine-2-carboxylic acid methyl ester* 4 :** To a solution of the amino acid derivative **3** (3.94 g, 8.94 mmol) in tetrahydrofuran (150 cm^3) was added dropwise triethylamine (2.48 cm^3, 17.88 mmol). The solution was heated under reflux for 16 h. The solvent was removed *in vacuo* and the residue dissolved in ethyl acetate (400 cm^3). The solution was washed with $NaHCO_3$ (10% w/v aq.) (200 cm^3), citric acid (10% w/v aq.) (200 cm^3) and water (200 cm^3). The organic phase was dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo*. The residue was chromatographed on silica gel with hexane-ethyl acetate (9:1) as the eluent to yield **4** as a white solid. (2.17 g, 90%), mp 71-74 C (from diethyl ether); (found: C, 53.57; H, 5.73; N, 5.13; S, 11.88. $C_{12}H_{15}NO_4S$ requires C, 53.52; H, 5.61; N, 5.21; S, 11.91%); υ_{max}(film)/cm^{-1} 2955 (CH), 1744 (C=O), 1328 and 1164 (SO_2); δ_H(400MHz, $CDCl_3$) 1.89 (3H, s, CH_3), 2.44 (3H, s, $C_4H_6C\underline{H}_3$), 2.71 (1H, s, one of CH_2), 2.79 (1H, s, one of CH_2) 3.75 (3H, s, CO_2CH_3), 7.33 (2H, d, *J* 8, Ar-H) and 7.84 (2H, d, *J* 8, Ar-H); *m/z* (CI) 270 (M+H, 24%), 238 (100), 155 (65), 114 (84) and 91 (26)

***2-Methyl-1-(toluene-4-sulphonyl)-aziridine-2-carboxylic acid* tert-*butyl ester* 1:** The methyl ester **4** (500 mg, 1.85 mmol) was dissolved in 1,4-dioxane (3 cm^3) and cooled to 0 C. A solution of lithium hydroxide monohydrate (78 mg, 1.85 mmol) in water (3 cm^3) was added dropwise. After 15 min the 1,4-dioxane was removed *in vacuo* and the aqueous solution extracted with dichloromethane (20 cm^3). The aqueous phase was acidified with HCl (1N), extracted with dichloromethane (2 x 20 cm^3) and the combined organic extracts dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo*. Recrystallisation from heptane-diethyl ether yielded the acid as a white solid.

***2-Methyl-1-(toluene-4-sulphonyl)-aziridine-2-carboxylic acid*.** (440 mg, 93%), mp 92-95 C (from heptane-diethyl ether); (found: C, 51.67; H, 5.23; N, 5.33; S, 12.50. $C_{11}H_{13}NO_4S$ requires C, 51.75; H, 5.13; N, 5.49; S, 12.56%); υ_{max}(film)/cm^{-1} 3242-2987 br (OH), 1721 (C=O), 1352 and 1161 (SO_2); δ_H(400MHz, $CDCl_3$) 1.94 (3H, s, CH_3), 2.45 (3H, s, $C_6H_4C\underline{H}_3$), 2.70 (1H, s, one of CH_2), 2.83 (1H, s, one of CH_2), 7.35 (2H, d, *J* 8, Ar-H) and 7.85 (2H, d, *J* 8, Ar-H); *m/z* (CI) 256 (M+H, 1%) 212 (100), 155 (94), 139 (30) and 91 (47); (found 256.064526. $C_{11}H_{14}NO_4S$ requires 256.064355).

A solution of *tert*-butyl 2,2,2-trichloroacetimidate (279 µl, 1.56 mmol) in cyclohexane (2 cm^3) was added to a solution of the acid (200 mg, 0.78 mmol) in tetrahydrofuran (2 cm^3) and cyclohexane (2 cm^3) at 0 C. Boron trifluoride etherate (15 µl, cat.) was added dropwise. After stirring for 30 min the reaction was quenched with solid $NaHCO_3$ (65 mg, 0.78 mmol). The solution was filtered through a plug of Celite® and concentrated *in vacuo*. The residue was chromatographed on silica gel with heptane-diethyl ether (7:3) as the eluent to yield **1** as a white solid. (204 mg, 84%), mp 65-67 C (from heptane-diethyl ether); (found: C, 57.50; H, 6.79; N, 4.43; S, 10.12. $C_{15}H_{21}NO_4S$ requires C, 57.86; H, 6.80; N, 4.50; S, 10.30%); υ_{max}(film)/cm^{-1} 2983, 2930 (CH), 1735 (C=O), 1329 and 1161 (SO_2);δ_H(400MHz, $CDCl_3$) 1.46 (9H, s, $CO_2C_4H_9$), 1.80 (3H, s, CH_3), 2.43 (3H, s, $C_6H_4C\underline{H}_3$), 2.62 (1H, s, one of CH_2), 2.77 (1H, s, one of CH_2), 7.32 (2H, d, *J* 8, Ar-H) and 7.84 (2H, d, *J* 8, Ar-H); *m/z* (CI) 312 (M+H, 3%), 256 (100), 238 (50), 155 (24) and 100 (26); (found 312.127717. $C_{15}H_{22}NO_4S$ requires 312.126955).

***Reaction of* 2-*Methyl*-1-(*toluene*-4-*sulphonyl*)-*aziridine*-2-*carboxylic acid* tert-*butyl ester* 1 *with nucleophiles*:**

***Table 1, entry 1*:** A solution of the aziridine carboxylate **1** (200 mg, 0.64 mmol) in diethyl ether (10 cm^3) was gradually added to a saturated ethereal solution of HCl, at 0 C. After stirring for 72 h at room temperature, the solvent was removed *in vacuo*. The residue was dissolved in diethyl ether (80 cm^3) and the solution washed with $NaHCO_3$ (10% w/v aq.) (40 cm^3). The organic phase was dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. The residue was chromatographed on silica gel with heptane-diethyl ether (9:1) as the eluent to yield a mixture of regioisomers resulting from C-3 and C-2 addition as white solids (194 mg, 87%) in a ratio of 1:4 respectively. ***3-Chloro-2-methyl-2-(toluene-4-sulphonylamino)-propionic acid* tert-*butyl ester*.** (39 mg, 17%), mp 51-53 C (from heptane-diethyl ether); (found: C, 51.56; H, 6.28; N, 3.89; Cl, 9.96. $C_{15}H_{22}NO_4SCl$ requires C, 51.79; H, 6.37; N, 4.02; Cl, 10.19%); υ_{max}(film)/cm^{-1} 3289 (NH), 1725 (C=O), 1296 and 1160 (SO_2);δ_H(400MHz, $CDCl_3$) 1.43 (3H, s, CH_3), 1.48 (9H, s, $CO_2C_4H_9$), 2.41 (3H, s, $C_6H_4C\underline{H}_3$), 3.33 (1H, d, *J* 12, one of CH_2), 3.69 (1H, d, *J* 12, one of CH_2), 5.62 (1H, s, $N\underline{H}SO_2C_6H_4$), 7.29 (2H, d, *J* 8, Ar-H) and 7.80 (2H, d, *J* 8, Ar-H); *m/z* (APCI) 312.5 (M-HCl, 100%). ***2-Chloro-2-methyl-3-(toluene-4-sulphonylamino)-propionic acid* tert-*butyl ester*.** (155 mg, 70%), mp 67-69 C (from heptane-diethyl ether); (found: C, 51.44; H, 6.35; N, 3.79; Cl, 9.89. $C_{15}H_{22}NO_4SCl$ requires C, 51.79; H, 6.37; N, 4.02; Cl, 10.19%); υ_{max}(film)/cm^{-1} 3283 (NH), 1744 (C=O), 1314 and 1164 (SO_2);δ_H(400MHz, $CDCl_3$) 1.51 (9H, s, $CO_2C_4H_9$), 1.69 (3H, s, CH_3), 2.41 (3H, s, $C_6H_4C\underline{H}_3$), 3.43 (2H, m, CH_2), 4.68 (1H, t, *J* 7, $N\underline{H}SO_2C_6H_4$), 7.30 (2H, d, *J* 8, Ar-H) and 7.76 (2H, d, *J* 8, Ar-H); *m/z* (APCI) 312.6 (M-HCl, 100%)

Table 1, entry 2: Formic acid (3 cm^3) was added to the aziridine carboxylate **1** (200 mg, 0.64 mmol) at 0 C and the reaction mixture stirred for 1.5 h. Evaporation of the excess formic acid yielded a mixture of regioisomers resulting from C-3 and C-2 addition (222 mg, 95%) in a ratio of 1:1 respectively. Attempts to separate these compounds by preparative chromatography were unsuccessful. ***3-Formyloxy-2-methyl-2-(toluene-4-sulphonylamino)-propionic acid* tert-*butyl ester***. δ_H(400MHz, $CDCl_3$) 1.54 (3H, s, CH_3), 1.59 (9H, s, $CO_2C_4H_9$), 2.41 (3H, s, $C_6H_4C\underline{H}_3$), 3.53 (2H, s, CH_2), 5.60 (1H, s, $N\underline{H}SO_2C_6H_4$), 7.30 (1H, d, *J* 8, Ar-H), 7.73 (2H, d, *J* 8, Ar-H) and 7.87 (1H, s, OCHO). ***2-Formyloxy-2-methyl-3-(toluene-4-sulphonylamino)-propionic acid* tert-*butyl ester***.δ_H(400MHz, $CDCl_3$) 1.44 (9H, s, $CO_2C_4H_9$), 1.50 (3H, s, CH_3), 2.43 (3H, s, $C_6H_4C\underline{H}_3$), 3.35 (2H, m, CH_2), 4.96 (1H, m, $N\underline{H}SO_2C_6H_4$), 7.31 (2H, d, *J* 8, Ar-H), 7.72 (2H, d, *J* 8, Ar-H) and 7.87 (1H, s, OCHO).

Table 1, entry 3: Benzylamine (42 μl, 0.39 mmol) was added to the aziridine carboxylate **1** (40 mg, 0.13 mmol) dissolved in tetrahydrofuran (10 cm^3). The reaction mixture was heated under reflux for 16 h. The solvent was removed *in vacuo* and the residue dissolved in ethyl acetate (20 cm^3). The organic phase was washed with brine (10 cm^3), dried ($MgSO_4$) and filtered. The solvent was evaporated *in vacuo* and the residue chromatographed on silica gel with heptane-diethyl ether (7:3) as the eluent to yield the regioisomer resulting from C-3 addition as a colourless gum. ***3-Benzylamino-2-methyl-2-(toluene-4-sulphonylamino)-propionic acid* tert-*butyl ester***. (45 mg, 84%), (found: C, 63.04; H, 7.26; N, 6.58; S, 7.52. $C_{22}H_{30}N_2O_4S$ requires C, 63.13; H, 7.22; N, 6.69; S, 7.66%); υ_{max}(film)/cm^{-1} 3346 br (NH), 2928 (CH), 1726 (C=O), 1333 and 1161 (SO_2);δ_H(400MHz, $CDCl_3$) 1.32 (3H, s, CH_3), 1.42 (9H, s, $CO_2C_4H_9$), 2.38 (3H, s, $C_6H_4C\underline{H}_3$), 2.79 (1H, d, *J* 12, one of CH_2), 2.85 (1H, d, *J* 12, one of CH_2), 3.63 (1H, d, *J* 14, one of $C_6H_5C\underline{H}_2NH$), 3.69 (1H, d, *J* 14, one of $C_6H_5C\underline{H}_2NH$), 6.01 (1H, s, $N\underline{H}SO_2C_6H_4$), 7.21-7.32 (7H, m, Ar-H) and 7.75 (2H, d, *J* 8, Ar-H); *m/z* (CI) 419 (M+H, 5%), 363 (63), 144 (22), 120 (100) and 91 (57); (found 419.201697. $C_{22}H_{31}N_2O_4S$ requires 419.200455).

Table 1, entry 4: Sodium azide (63 mg, 0.96 mmol) was added to a solution of the aziridine carboxylate **1** (100 mg, 0.32 mmol) in dimethylformamide (2 cm^3). After stirring for 72 h at room temperature, the solvent was removed *in vacuo*. The residue was dissolved in ethyl acetate (20 cm^3) and washed with $NaHCO_3$ (10% w/v aq.) (20 cm^3). The aqueous phase was extracted with ethyl acetate (2 x 20 cm^3). The combined organic phases were dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo*. The residue was chromatographed on silica gel with heptane-diethyl ether (9:1) as the eluent to yield a mixture of regioisomers resulting from C-3 and C-2 addition as white solids (85 mg, 75%) in a ratio of 1:4 respectively. ***3-Azido-2-methyl-2-(toluene-4-sulphonylamino)-propionic acid* tert-*butyl ester***. (17 mg, 15%), mp 105-107 C (from heptane-diethyl ether); (found: C, 50.87; H, 6.28; N, 15.62; S, 9.06. $C_{15}H_{22}N_4O_4S$ requires C, 50.83; H, 6.26; N, 15.81; S, 9.05%);υ_{max}(film)/cm^{-1} 3282 (NH), 2106 (N_3), 1729 (C=O), 1329 and 1160 (SO_2);δ_H(400MHz, $CDCl_3$) 1.37 (3H, s, CH_3), 1.46 (9H, s, $CO_2C_4H_9$), 2.41 (3H, s, $C_6H_4C\underline{H}_3$), 3.49 (1H, d, *J* 12, one of CH_2), 3.82 (1H, d, *J* 12, one of CH_2), 5.64 (1H, s, $N\underline{H}SO_2C_6H_4$), 7.29 (2H, d, *J* 8, Ar-H) and 7.78 (2H, d, *J* 8, Ar-H); *m/z* (CI) 355 (M+H, 1%), 253 (100), 242 (80), 155 (82) and 99 (88).***2-Azido-2-methyl-3-(toluene-4-sulphonylamino)-propionic acid* tert-*butyl ester***. (68 mg, 60%), mp 70-72 C (from heptane-diethyl ether); (found: C, 50.90; H, 6.35; N, 15.44; S, 8.54. $C_{15}H_{22}N_4O_4S$ requires C, 50.83; H, 6.26; N, 15.81; S, 9.05%);υ_{max}(film)/cm^{-1} 3283 (NH), 2120 (N_3), 1734 (C=O), 1334 and 1164 (SO_2);δ_H(400MHz, $CDCl_3$) 1.49 (9H, s, $CO_2C_4H_9$), 1.51 (3H, s, CH_3), 2.43 (3H, s, $C_6H_4C\underline{H}_3$), 2.97 (1H, dd, *J* 7 and 12, one of CH_2), 3.13 (1H, dd, *J* 7 and 12, one of CH_2), 4.78 (1H, t, *J* 7, $N\underline{H}SO_2C_6H_4$), 7.30 (2H, d, *J* 8, Ar-H) and 7.72 (2H, d, *J* 8, Ar-H); *m/z* (CI) 355 (M+H, 6%) 299 (93), 184 (100), 155 (86) and 116 (68).

Table 1, entry 5: These compounds were prepared following the procedure described above (table 1, entry 4) using the aziridine **1** (100 mg, 0.32 mmol), thiophenol (66 μl, 0.64 mmol) and dimethylformamide (2 cm^3). The residue was chromatographed on silica gel with heptane-ethyl acetate (9:1) to yield a mixture of regioisomers resulting from C-3 and C-2 addition as a gum and as a white solid (115 mg, 85%) in a ratio of 1:1 respectively. ***2-Methyl-3-phenylsulphanyl-2-(toluene-4-sulphonylamino)-propionic acid* tert-*butyl ester***. (57 mg, 42%); (found: C, 59.88; H, 6.49; N, 3.31; S, 14.96. $C_{21}H_{27}NO_4S_2$ requires C, 59.83; H, 6.46; N, 3.32; S, 15.21%);υ_{max}(film)/cm^{-1} 3282 (NH), 2980 (CH), 1727 (C=O), 1331 and 1156 (SO_2);δ_H(400MHz, $CDCl_3$) 1.38 (9H, s, $CO_2C_4H_9$), 1.48 (3H, s, CH_3), 2.39 (3H, s, $C_6H_4C\underline{H}_3$), 3.31 (1H, d, *J* 13, one of CH_2), 3.50 (1H, d, *J* 13, one of CH_2), 5.64 (1H, s, $N\underline{H}SO_2C_6H_4$), 7.18-7.73 (7H, m, Ar-H) and 7.74 (2H, d, *J* 8, Ar-H); *m/z* (CI) 421 (M+, 2%), 366 (15), 320 (13), 242 (20) and 195 (100); (found 422.145292. $C_{21}H_{28}NO_4S_2$ requires 422.145977). ***2-Methyl-2-phenylsulphanyl-3-(toluene-4-sulphonylamino)-propionic acid* tert-*butyl ester***. (58 mg, 43%), mp 107-108 C (from heptane-diethyl ether); (found: C, 59.82; H, 6.59; N, 3.30; S, 14.98. $C_{21}H_{27}NO_4S_2$ requires C, 59.83; H, 6.46; N, 3.32; S, 15.21%);υ_{max}(film)/cm^{-1} 3283 br (NH), 2979 (CH), 1723 (C=O), 1333 and 1164 (SO_2);δ_H(400MHz, $CDCl_3$) 1.40 (9H, s, $CO_2C_4H_9$), 1.42 (3H, s, CH_3), 2.44 (3H, s, $C_6H_4C\underline{H}_3$), 3.08 (1H, dd, *J* 7 and 13, one of CH_2), 3.16 (1H, dd, *J* 7 and 13, one of CH_2), 4.95 (1H, t, *J* 7, $N\underline{H}SO_2C_6H_4$), 7.21-

7.36 (7H, m, Ar-H) and 7.71 (2H, d, *J* 8, Ar-H); *m/z* (CI) 422 (M+H, 1%), 366 (42), 195 (100), 182 (53) and 111 (32); (found 422.146029. $C_{21}H_{28}NO_4S_2$ requires 422.146001).

Table 1, entry 6: Copper bromide-dimethylsulfide complex ($CuBr.SMe_2$) (12 mg, 0.2%/mmol) was added to a solution of aziridine carboxylate **1** (90 mg, 0.28 mmol) in tetrahydrofuran (3 cm^3). The solution was cooled to -40 C and then isopropylmagnesium chloride (0.7 cm^3 of a 2 mol dm^{-3} solution in diethyl ether, 1.44 mmol) was added dropwise. The reaction was stirred at -40 C for 1h, allowed to warm to room temperature and then heated under reflux for 1 h. The reaction was quenched with NH_4Cl (sat. aq.) (20 cm^3) and the aqueous phase extracted with ethyl acetate (2 x 20 cm^3). The combined organic phases were washed with brine (20 cm^3), dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo*. The residue was chromatographed on silica gel with heptane-diethyl ether (4:1) as the eluent to yield the regioisomer resulting from C-3 addition as a white solid. **2,4-*Dimethyl*-2-(*toluene*-4-*sulphonylamino*)-*pentanoic acid* tert-*butyl ester***. (61 mg, 60%), mp 69-71 C (from heptane-diethyl ether), (found: C, 61.02; H, 8.31; N, 3.88; S, 8.84. $C_{18}H_{29}NO_4S$ requires C, 60.82; H, 8.22; N, 3.94; S, 9.02%); υ_{max}(film)/cm^{-1} 3287(NH), 2959, 2873 (CH), 1732 (C=O), 1327 and 1151 (SO_2);δ_H(400MHz, $CDCl_3$) 0.85 (3H, d, *J* 6, three of $CH(C\underline{H}_3)_2$), 0.94 (3H, d, *J* 7, three of $CH(C\underline{H}_3)_2$), 1.30 (3H, s, CH_3), 1.44 (9H, s, $CO_2C_4H_9$), 1.58 (1H, dd, *J* 6 and 14, one of $CHC\underline{H}_2$), 1.82 (1H, m, $C\underline{H}CH_2$), 1.92 (1H, dd, *J* 6 and 14, one of $CHC\underline{H}_2$), 2.40 (3H, s, $C_6H_4C\underline{H}_3$), 5.53 (1H, s, $N\underline{H}SO_2C_6H_4$), 7.27 (2H, d, *J* 7, Ar-H) and 7.75 (2H, d, *J* 7, Ar-H); *m/z* (CI) 356 (M+H, 1%), 300 (77), 255 (26), 254 (100) and 100 (43); (found 356.190353. $C_{18}H_{30}NO_4S$ requires 356.189556).

Table 1, entry 7: This compound was prepared following the procedure described above (table 1, entry 6) using **1** (80 mg, 0.25 mmol), phenylmagnesium bromide (426 µl of a 3 mol dm^{-3} solution in tetrahydrofuran, 1.28 mmol), copper bromide-dimethylsulfide complex (10 mg, 0.2%/mmol) and tetrahydrofuran (3 cm^3). The residue was chromatographed on silica gel with heptane-diethyl ether (9:1) as the eluent to yield the regioisomer resulting from C-3 addition as a colourless gum. **2-*Methyl*-3-*phenyl*-2-(*toluene*-4-*sulphonylamino*)-*propionic acid* tert-*butyl ester***. (52 mg, 52%), (found: C, 64.57; H, 6.90; N, 3.49; S, 8.05. $C_{21}H_{27}NO_4S$ requires C, 64.76; H, 6.99; N, 3.60; S, 8.23%);υ_{max}(film)/cm^{-1} 3278 (NH), 1727 (C=O), 1279 and 1158 (SO_2);δ_H(400MHz, $CDCl_3$) 1.37 (9H, s, $CO_2C_4H_9$), 1.41 (3H, s, CH_3), 2.40 (3H, s, $C_6H_4C\underline{H}_3$), 2.99 (1H, d, *J* 14, one of CH_2), 3.22 (1H, d, *J* 14, one of CH_2), 5.30 (1H, s, $N\underline{H}SO_2C_6H_4$), 7.23-7.30 (7H, m, Ar-H) and 7.74 (2H, d, *J* 8, Ar-H), *m/z* (APCI) 390 (M+H, 27%), 334 (100) and 256 (21); (found 390.1739. $C_{21}H_{28}NO_4S$ requires 390.1739).

Table 1, entry 8: Ethylmagnesium chloride (560 µl of a 3 mol dm^{-3} solution in diethyl ether, 1.76 mmol) in tetrahydrofuran (5 cm^3) was cooled to 0 C and indole (188 mg, 1.60 mmol) was added portionwise. The reaction mixture was then heated under reflux for 2 h and allowed to cool to room temperature. The solution was added dropwise to a cooled (-40 C) solution **1** (100 mg, 0.32 mmol) and copper bromide-dimethylsulfide complex (14 mg, 0.2% /mmol) in tetrahydrofuran (5 cm^3). The reaction mixture was allowed to warm to room temperature and heated under reflux for 16 h, cooled to room temperature and quenched with NH_4Cl (sat. aq.) (40 cm^3). The aqueous phase was extracted with ethyl acetate (2 x 40 cm^3). The combined organic phases were washed with brine (20 cm^3), dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo*. The residue was chromatographed on silica gel with heptane-diethyl ether (1:1) as the eluent to yield the regioisomer resulting from C-3 addition as a white solid. **3-(1H-*Indol*-3-yl)-2-*methyl*-2-(*toluene*-4-*sulphonylamino*)-*propionic acid* tert-*butyl ester***. (66 mg, 48%), mp 53-55 C (from heptane-diethyl ether); (found: C, 64.62; H, 6.66; N, 6.31. $C_{23}H_{28}N_2O_4S$ requires C, 64.46; H, 6.59; N, 6.54%); υ_{max}(film)/cm^{-1} 3395 br (NH), 1722 (C=O), 1317 and 1157 (SO_2);δ_H(400MHz, $CDCl_3$) 1.25 (9H, s, $CO_2C_4H_9$), 1.48 (3H, s, CH_3), 2.38 (3H, s, $C_6H_4C\underline{H}_3$), 3.21 (1H, d, *J* 15, one of CH_2), 3.34 (1H, d, *J* 15, one of CH_2), 5.48 (1H, s, $N\underline{H}SO_2C_6H_4$), 7.08-7.26 (5H, m, Ar-H and Ind(2)H), 7.34 (1H, d, *J* 8, Ar-H), 7.61 (1H, d, *J* 8, Ar-H), 7.74 (2H, d, *J* 8, Ar-H) and 8.06 (1H, br, Ind-NH); *m/z* (CI) 428 (M+, 1%), 373 (13), 202 (28), 131 (13) and 130 (100).

(S)-1-*Azido*-3-(tert-*butyl*-*diphenyl*-*silanyloxy*)-2-*methyl*-*propan*-2-*ol* (S)-**7** :*tert*-Butyldiphenylsilylchloride (7.10 cm^3, 27.20 mmol) in dichloromethane (3 cm^3) was cannulated over 40 min into a stirred solution of (R)-2-methyl-glycidol **6** (2.00 g, 22.70 mmol), 4-dimethylaminopyridine (cat.), and imidazole (1.70g, 25.00 mmol) in dichloromethane (60 cm^3) at 0 C. The solution was stirred for 3h. The reaction mixture was diluted with dichloromethane (400 cm^3), washed with water (3 x 100 cm^3), and the aqueous washes back extracted with dichloromethane (100 cm^3). The combined organic phases were washed with NH_4Cl (sat. aq.) (100 cm^3), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The residual oil was chromatographed on silica gel with heptane-diethyl ether (95:5) as the eluent to yield the title compoud as a colourless oil. **(S)-tert-*Butyl*-(2-*methyl*-*oxiranylmethoxy*)-*diphenyl*-*silane***. (7.33 g, 99%), $[\alpha]_D^{20}$ 7.96 (c 1.0 in CH_2Cl_2); (found: C, 73.52; H, 7.95. $C_{20}H_{26}O_2Si$ requires C, 73.57; H, 8.03%);υ_{max}(film)/cm^{-1} 2931, 2858 (CH) and 1113 (SiO);δ_H(400MHz, $CDCl_3$) 1.06 (9H, s, C_4H_9), 1.37

(3H, s, CH_3), 2.57 (1H, d, *J* 5, one of CH_2), 2.69 (1H, d, *J* 5, one of CH_2), 3.64 (1H, d, *J* 11, one of CH_2OSi), 3.67 (1H, d, *J* 11, one of CH_2OSi), 7.35-7.44 (6H, m, Ar-H) and 7.67 (4H, m, Ar-H); *m/z* (CI) 327 (M+H, 4%), 296 (56), 239 (79), 199 (45) and 191 (100); (found 327.175553. $C_{20}H_{27}O_2Si$ requires 327.178034).To the epoxy ether (1.00 g, 3.06 mmol) in methanol (100 cm^3) was added sodium azide (796 mg, 12.25 mmol) and NH_4Cl (655 mg, 12.25 mmol) in methanol (100 cm^3) and water (20 cm^3). The reaction mixture was heated under reflux for 3 h. The solvent was removed *in vacuo* and the reaction mixture poured into a solution of ethyl acetate (200 cm^3), and brine (100 cm^3). The aqueous phase was extracted with ethyl acetate (2 x 100 cm^3). The combined organic phases were washed with brine (100 cm^3), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude oil was chromatographed on silica gel with heptane-diethyl ether (9:1) as the eluent to yield **(S)-7** as a colourless oil. (1.11 g, 99%), $[\alpha]_D^{20}$ -17.70 (c 1.1 in CH_2Cl_2); (found: C, 65.23; H, 7.37; N, 10.83. $C_{20}H_{27}N_3O_2Si$ requires C, 65.01; H, 7.36; N, 11.37%);υ_{max}(film)/cm^{-1} 3445 br (OH), 2932, 2859 (CH), 2103 (N_3) and 1113 (SiO); δ_H(400MHz, $CDCl_3$) 1.08 (9H, s, C_4H_9), 1.18 (3H, s. CH_3), 2.45 (1H, s, OH), 3.33 (1H, d, *J* 12, one of CH_2), 3.37 (1H, d, *J* 12, one of CH_2), 3.48 (1H, d, *J* 10, one of CH_2OSi), 3.56 (1H, d, *J* 10, one of CH_2OSi), 7.38-7.47 (6H, m, Ar-H) and 7.64 (4H, m, Ar-H); *m/z* (CI) 235 (72), 199 (100), 179 (74) and 117 (77); (found 392.175698. $C_{20}H_{27}N_3O_2SiNa$ requires 392.177025).

(R)-2-(tert-*Butyl-diphenyl-silanylmethyl*)-2-*methyl*-1-(*toluene*-4-*sulphonyl*)-*aziridine* (R)-5 :Triphenylphosphine (234 mg, 0.89 mmol) was added to a stirred solution of azido alcohol **(S)-7** (300 mg, 0.81 mmol) in tetrahydrofuran (20 cm^3). The reaction was stirred at room temperature for 1 h and then heated under reflux for 5 h. After cooling, triethylamine (226 µl, 1.62 mmol) and *p*-toluenesulphonyl chloride (308 mg, 1.62 mmol) were added to the mixture at 0 C, and the reaction mixture stirred at room temperature for 4 h. The solvent was removed *in vacuo* and the residual paste dissolved in ethyl acetate (60 cm^3). The solution was washed with copper sulphate (10% w/v aq.) (30 cm^3), citric acid (10% w/v aq.) (30 cm^3) and water (30 cm^3). The organic phase was dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo*. The residue was chromatographed on silica gel with heptane-diethyl ether (1:1) as the eluent to yield **(R)-5** as a white solid. (214 mg, 55%), mp 78-80 C (from heptane-diethyl ether); $[\alpha]_D^{22}$ +23.2 (c 1.0 in CH_2Cl_2); (found: C, 67.59; H, 7.01; N, 2.89; S, 6.19. $C_{27}H_{33}NO_3SSi$ requires C, 67.60; H, 6.93; N, 2.92; S, 6.68%);υ_{max}(film)/cm^{-1} 2931, 2858 (CH), 1323, 1162 (SO_2) and 1113 (SiO);δ_H(400MHz, $CDCl_3$) 1.00 (9H, s, C_4H_9), 1.74 (3H, s. CH_3), 2.25 (1H, s, one of CH_2), 2.41 (3H, s, $C_6H_4C\underline{H}_3$), 2.59 (1H, s, one of CH_2), 3.58 (1H, d, *J* 11, one of CH_2OSi), 3.70 (1H, d, *J* 11, one of CH_2OSi), 7.25-7.34 (2H, m, Ar-H), 7.36-7.44 (6H, m, Ar-H), 7.63 (4H, m, Ar-H) and 7.82 (2H, d, *J* 8, Ar-H); *m/z* (CI) 480 (M+H, 1%), 344 (68), 309 (100), 199 (75) and 91 (74); (found 502.183801. $C_{27}H_{33}NO_3SSiNa$ requires 502.184814).

***Reaction of* (R)-2-(tert-*Butyl-diphenyl-silanylmethyl*)-2-*methyl*-1-(*toluene*-4-*sulphonyl*)-*aziridine* (R)-5 *with nucleophiles*:**

Table 2, entry 1: A solution of aziridine **(R)-5** (100 mg, 0.37 mmol) in diethyl ether (5 cm^3) was gradually added to a saturated ethereal solution of HCl at 0 C. After stirring for 72 h at room temperature, the solvent was removed *in vacuo*. The residue was dissolved in diethyl ether (40 cm^3) and washed with $NaHCO_3$ (10% w/v aq) (20 cm^3). The organic phase was dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo*. The mixture was chromatographed on silica gel with heptane-ethyl acetate (4:1) as the eluent to yield a mixture of regioisomers resulting from C-3 and C-2 addition as a colourless gum and as a white solid (101 mg, 95%) in a ratio of 1:1.25 respectively. **(S)-N-[1-(tert-*Butyl-diphenyl-silanyloxymethyl*)-2-*chloro*-1-*methyl-ethyl*]-4-*methyl-benzene sulphonamide***. (45 mg, 42%), $[\alpha]_D^{21}$ -1.2 (c 0.6 in CH_2Cl_2); (found: C, 63.05; H, 6.65; N, 2.72; Cl, 6.83; S, 6.44. $C_{27}H_{34}NO_3ClSSi$ requires C, 62.83; H, 6.64; N, 2.71; Cl, 6.87; S, 6.21%);υ_{max}(film)/cm^{-1} 3278 (NH), 2931, 2858 (CH), 1329, 1162 (SO_2) and 1113 (SiO);δ_H(400MHz, $CDCl_3$) 1.07 (9H, s, C_4H_9), 1.19 (3H, s, CH_3), 2.40 (3H, s, $C_6H_4C\underline{H}_3$), 3.40 (1H, d, *J* 10, CH_2), 3.65 (1H, d, *J* 10, CH_2), 3.67 (1H, d, *J* 11, one of CH_2OSi), 3.77 (1H, d, *J* 11, one of CH_2OSi), 5.05 (1H, s, $N\underline{H}SO_2C_6H_4$), 7.22-7.29 (2H, m, Ar-H), 7.36-7.48 (6H, m, Ar-H) and 7.60-7.69 (6H, m, Ar-H); *m/z* (APCI) 516.5 (M+H, 13%), 440.4 (43) and 438.3 (100); (found 538.163293. $C_{27}H_{34}NO_3ClSSiNa$ requires 538.161492).**(S)-N-[3-[tert-*Butyl-diphenyl-silanyloxy*)-2-*chloro*-2-*methyl-propyl*]-4-*methyl-benzene sulphonamide***. (56 mg, 53%), mp 92-93 C (from heptane-diethyl ether); $[\alpha]_D^{22}$ +8.3 (c 0.8 in CH_2Cl_2); (found: C, 62.84; H, 6.67; N, 2.70; Cl, 6.91; S, 6.03. $C_{27}H_{34}NO_3ClSSi$ requires C, 62.83; H, 6.64; N, 2.71; Cl, 6.87; S, 6.21%);υ_{max}(film)/cm^{-1} 3279 (NH), 1334, 1165 (SO_2) and 1113 (SiO);δ_H(400MHz, $CDCl_3$) 1.04 (9H, s, C_4H_9), 1.52 (3H, s, CH_3), 2.42 (3H, s, $C_6H_4C\underline{H}_3$), 3.20 (1H, dd, *J* 7 and 13, CH_2), 3.28 (1H, dd, *J* 7 and 13, CH_2), 3.61 (1H, d, *J* 10, one of CH_2OSi), 3.72 (1H, d, *J* 10, one of CH_2OSi), 4.72 (1H, t, *J* 7, $N\underline{H}SO_2C_6H_4$), 7.29 (2H, d, *J* 8, Ar-H), 7.37-7.45 (6H, m, Ar-H), 7.59-7.63 (4H, m, Ar-H) and 7.71 (2H, d, *J* 8, Ar-H); (found 516.180072. $C_{27}H_{35}NO_3ClSSi$ requires 516.179547).

Table 2, entry 2: Formic acid (3 cm^3) was added to the aziridine **(R)-5** (300 mg, 0.63 mmol) at 0 C and the reaction mixture stirred for 1 h. After evaporation of excess formic acid the residue was chromatographed on silica gel with heptane-ethyl acetate (7:3) as the eluent to yield the regioisomer resulting from C-2 addition as colourless needles. **(S)-*Formic acid*-2-(*tert-butyl-diphenyl-silanyloxymethyl*)-1-*methyl*-1-[(*toluene-4-sulphonyl amino*)-*methyl*]-*ethyl ester***. (256 mg, 78%), mp 107-108 C (from heptane-diethyl ether); $[\alpha]_D^{24}$ -6.9 (c 1.0 in CH_2Cl_2); (found: C, 64.01; H, 6.85; N, 2.90; S, 6.08. $C_{28}H_{35}NO_5SSi$ requires C, 63.96; H, 6.71; N, 2.66; S, 6.09%); υ_{max}(film)/cm^{-1} 3281 br (NH, CHO), 1724 (CO), 1332, 1163 (SO_2) and 1164 (SiO); δ_H(400MHz, $CDCl_3$) 1.03 (9H, s, C_4H_9), 1.44 (3H, s, CH_3), 2.42 (3H, s, $C_6H_4C\underline{H}_3$), 3.25 (1H, dd, *J* 6 and 13, one of CH_2), 3.33 (1H, dd, *J* 6 and 13, one of CH_2), 3.68 (1H, d, *J* 10, one of CH_2OSi), 3.84 (1H, d, *J* 10, one of CH_2OSi), 4.96 (1H, t, *J* 6, $N\underline{H}SO_2C_6H_4$), 7.26 (2H, m, Ar-H), 7.36-7.47 (6H, m, Ar-H), 7.58 (4H, m, Ar-H), 7.68 (2H, d, *J* 8, Ar-H) and 7.86 (1H, s, OCHO); (found 543.2350. $C_{28}H_{39}N_2O_5SSi$ requires 543.2351).

Table 2, entry 3: Benzylalcohol (65 µl, 0.62 mmol) was added to a cooled solution (0 C) of the aziridine **(R)-5** (100 mg, 0.20 mmol) in dichloromethane (5 cm^3), followed by boron trifluoride etherate (20 µ, cat.). After stirring for 16 h at room temperature, the reaction was quenched with $NaHCO_3$ (10 %w/v aq.) (10 cm^3). The aqueous phase was extracted with ethyl acetate (2 x 10 cm^3), the combined organic phases dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo*. The residue was chromatographed on silica gel with heptane-diethyl ether (1:1) as the eluent to yield the regioisomer resulting from C-2 addition as a colourless gum. **(S)-N-[2-*Benzyloxy*-3-(*tert-butyl-diphenyl-silanyloxy*)-2-*methyl-propyl*]-4-*methyl-benzene sulfonamide***. (87 mg, 67%), $[\alpha]_D^{22}$ +7.9 (c 1.1 in CH_2Cl_2); (found: C, 69.49; H, 7.29; N, 2.26; S, 5.15. $C_{34}H_{41}NO_4SSi$ requires C, 69.46; H, 7.03; N, 2.38; S, 5.45%);υ_{max}(film)/cm^{-1} 3284 (NH), 1428 (C-$(CH_3)_3$), 1331 and 1113 (SO_2, SiO);δ_H(400MHz, $CDCl_3$) 1.02 (9H, s, C_4H_9), 1.26 (3H, s, CH_3), 2.40 (3H, s, $C_6H_4C\underline{H}_3$), 3.04 (1H, dd, *J* 6 and 12, one of CH_2), 3.17 (1H, dd, *J* 6 and 12, one of CH_2), 3.52 (1H, d, *J* 11, one of CH_2OSi), 3.67 (1H, d, *J* 11, one of CH_2OSi), 4.34 (2H, s, $C\underline{H}_2OPh$), 4.75 (0.5H, d, *J* 6, $N\underline{H}SO_2C_6H_4$), 4.77 (0.5H, d, *J* 6, $N\underline{H}SO_2C_6H_4$), 7.18-7.43 (13H, m, Ar-H) and 7.58-7.69 (6H, m, Ar-H); *m/z* (APCI) 588.5 (M+H, 100%) and 274.1 (68).

Table 2, entry 4: Benzylamine (341 µl, 3.13 mmol) was added to the aziridine **(R)-5** (300 mg, 0.62 mmol) dissolved in tetrahydrofuran (20 cm^3). The reaction mixture was heated to reflux for 16 h. The solvent was evaporated *in vacuo* and the residue dissolved in ethyl acetate (60 cm^3), washed with brine (30 cm^3), dried ($MgSO_4$) and filtered. The solvent was evaporated *in vacuo* and the residue chromatographed on silica gel with heptane-diethyl ether (4:1) as the eluent to yield the regioisomer resulting from C-3 addition as a colourless gum.**(R)-N-[2-*Benzylamino*-1-(*tert-butyl-diphenyl-silanyloxymethyl*)-1-*methyl-ethyl*]-4-*methyl-benzenesulphonamide***. (353 mg, 96%), $[\alpha]_D^{22}$ -1.0 (c 1.4 in CH_2Cl_2); (found: C, 69.74; H, 7.29; N, 4.50; S, 5.23. $C_{34}H_{42}N_2O_3SSi$ requires C, 69.59; H, 7.21; N, 4.77; S, 5.46%);υ_{max}(film)/cm^{-1} 3281 (NH), 1326, 1161 (SO_2) and 1113 (SiO); δ_H(400MHz, $CDCl_3$) 1.03 (9H, s, C_4H_9), 1.08 (3H, s, CH_3), 2.33 (1H, d, *J* 12, one of CH_2), 2.37 (3H, s, $C_6H_4C\underline{H}_3$), 2.76 (1H, d, *J* 12, one of CH_2), 3.46 (1H, d, *J* 10, one of CH_2OSi), 3.60 (1H, d, *J* 10, one of CH_2OSi), 3.62 (2H, s, $PhC\underline{H}_2NH$), 5.29 (1H, s, $N\underline{H}SO_2C_6H_4$), 7.17 (4H, m, Ar-H), 7.20-7.42 (9H, m, Ar-H), 7.56 (4H, m, Ar-H) and 7.62 (2H, d, *J* 8, Ar-H); *m/z* (APCI) 587 (M+H, 100%).

Table 2, entry 5: Sodium azide (81 mg, 1.25 mmol) was added to a solution of the aziridine **(R)-5** (200 mg, 0.41 mmol) in dimethylformamide (2 cm^3). After stirring for 72 h at room temperature, the solvent was evaporated. The residue was dissolved in ethyl acetate (40 cm^3) and washed with $NaHCO_3$ (10% w/v aq.) (20 cm^3). The aqueous phase was extracted with ethyl acetate (20 cm^3), the combined extracts were dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. The residue was chromatographed on silica gel with heptane-diethyl ether (9:1) as the eluent to yield the regioisomer resulting from C-3 addition as a colourless gum.**(S)-N-[2-*Azido*-1-(*tert-butyl-diphenyl-silanyloxymethyl*)-1-*methyl-ethyl*]-4-*methyl-benzene sulphonamide***. (196 mg, 90%), $[\alpha]_D^{21}$ -13.9 (c 1.5 in CH_2Cl_2); (found: C, 61.81; H, 6.62; N, 10.59; S, 6.00. $C_{27}H_{34}N_4O_3SSi$ requires C, 62.04; H, 6.56; N, 10.72; S, 6.13%);υ_{max}(film)/cm^{-1} 3266 (NH), 2106 (N_3), 1327, 1160 (SO_2) and 1093 (SiO);δ_H(400MHz, $CDCl_3$) 1.07 (9H, s, C_4H_9), 1.10 (3H, s, CH_3), 2.40 (3H, s, $C_6H_4C\underline{H}_3$), 3.37 (1H, d, *J* 10, one of CH_2OSi), 3.48 (1H, d, *J* 12, one of CH_2), 3.54 (1H, d, *J* 10, one of CH_2OSi), 3.56 (1H, d, *J* 12, one of CH_2), 4.95 (1H, s, $N\underline{H}SO_2C_6H_4$), 7.22-7.25 (2H, m, Ar-H), 7.39-7.46 (6H, m, Ar-H), 7.58-7.62 (4H, m, Ar-H) and 7.67 (2H, d, *J* 8, Ar-H); *m/z* (CI) 523 (M+H, 1%), 446 (30), 445 (100), 388 (28) and 91 (30).

Table 2, entry 6: This compound was prepared following the procedure described above (table 2, entry 5) using (R)-2-(*tert*-butyl-diphenyl-silanylmethyl)-2-methyl-1-(toluene-4-sulphonyl)-aziridine **(R)-5** (150 mg, 0.31 mmol), thiophenol (64 µl, 0.62 mmol) and dimethylformamide (2 cm^3). The residue was chromatographed on silica gel with heptane-ethyl acetate (9:1) as the eluent to

yield the regioisomer resulting from C-3 addition as a colourless gum. **(S)-N-[1-(tert-*Butyl-diphenyl-silanyloxymethyl*)-1-*methyl-2-phenylsuphanyl-ethyl*]-4-*methyl-benzenesulphonamide***. (135 mg, 90%), $[\alpha]_D^{21}$ -12.9 (c 0.4 in CH_2Cl_2); (found: C, 67.44; H, 6.76; N, 2.32; S, 10.59. $C_{33}H_{39}NO_3S_2Si$ requires C, 67.19; H, 6.66; N, 2.37; S, 10.87%);υ_{max}(film)/cm^{-1} 3278 (NH), 1327, 1159 (SO_2) and 1091 (SiO);δ_H(400MHz, $CDCl_3$) 1.05 (9H, s, C_4H_9), 1.14 (3H, s, CH_3), 2.38 (3H, s, $C_6H_4C\underline{H}_3$), 3.19 (1H, d, *J* 13, one of CH_2), 3.40 (1H, d, *J* 13, one of CH_2), 3.43 (1H, d, *J* 10, one of CH_2OSi), 3.67 (1H, d, *J* 10, one of CH_2OSi), 5.29 (1H, s, $N\underline{H}SO_2C_6H_4$), 7.14-7.30 (5H, m, Ar-H), 7.34-7.46 (7H, m, Ar-H) and 7.55-7.64 (7H, m, Ar-H); *m/z* (CI) 590 (M+H, 10%), 512 (22), 419 (34) and 341 (100); (found 612.202891. $C_{33}H_{39}NO_3S_2SiNa$ requires 612.203836).

Table 2, entry 7: To a solution of the aziridine **(R)-5** (300 mg, 0.62 mmol) in tetrahydrofuran (15 cm^3) was added copper bromide-dimethylsulfide (25 mg, 0.2%/mmol). The solution was cooled to -40 C before dropwise addition of isopropylmagnesium chloride (1.56 cm^3 of a 2 mol dm^{-3} solution in diethyl ether, 3.13 mmol). The reaction was stirred at -40 C for 1h, allowed to warm to room temperature and then heated under reflux for 1 h. The reaction was quenched with NH_4Cl (sat. aq.) (60 cm^3) and the aqueous phase was extracted with ethyl acetate (2 x 60 cm^3). The combined organic extracts were washed with brine (30 cm^3), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The residue was chromatographed on silica gel with heptane-ethyl acetate (9:1) as the eluent to yield the regioisomer resulting from C-3 addition as a gum.**(R)-N-[1-(tert-*Butyl-diphenyl-silanyloxymethyl*)-1,3dimethyl-butyl]-4-*methyl-benzene sulphonamide***. (253 mg, 78%), $[\alpha]_D^{18}$ +5.0 (c 1.0 in CH_2Cl_2); (found: C, 68.85; H, 7.82; N, 2.57; S, 6.62. $C_{30}H_{41}NO_3SSi$ requires C, 68.79; H, 7.89; N, 2.67; S, 6.12%); υ_{max}(film)/cm^{-1} 3280 (NH), 1323, 1151 (SO_2) and 1113 (SiO);δ_H(400MHz, $CDCl_3$) 0.85 (3H, d, *J* 6, three of $CH(C\underline{H}_3)_2$), 0.89 (3H, d, *J* 6, three of $CH(C\underline{H}_3)_2$), 1.08 (9H, s, C_4H_9), 1.43 (1H, dd, *J* 6 and 15, one of CH_2), 1.56 (1H, dd, *J* 6 and 15, one of CH_2), 1.65 (1H, m, $C\underline{H}(CH_3)_2$), 2.40 (3H, s, $C_6H_4C\underline{H}_3$), 3.39 (2H, s, CH_2OSi), 4.85 (1H, s, $N\underline{H}SO_2C_6H_4$), 7.20 (2H, d, *J* 8, Ar-H), 7.36-7.45 (6H, m, Ar-H), 7.59-7.61 (4H, m, Ar-H) and 7.69 (2H, d, *J* 8, Ar-H); (found 524.2655. $C_{30}H_{42}NO_3SSi$ requires 524.2655).

Table 2, entry 8: This compound was prepared following the procedure described above (table 2, entry 7) using **(R)-5** (300 mg, 0.63 mmol), phenylmagnesium bromide (3.13 cm^3 of a 1 mol dm^{-3} solution in diethyl ether, 3.13 mmol), copper bromide-dimethylsulfide (15 mg, 0.2%/mmol), tetrahydrofuran (25 cm^3). The residue was chromatographed on silica gel with heptane-ethyl acetate (9:1) as the eluent to yield the regioisomer resulting from C-3 addition as a white solid.**(R)-N-[1-(tert-*Butyl-diphenyl-silanyloxymethyl*)-1-*methyl-2-phenyl-ethyl*]-4-*methyl-benzene sulphonamide***. (263 mg, 75%), mp 112-115 C (from heptane-diethyl ether); $[\alpha]_D^{20}$ +9.6 (c 1.0 in CH_2Cl_2); (found: C, 71.17; H, 7.07; N, 2.51; S, 5.86. $C_{33}H_{39}NO_3SSi$ requires C, 71.06; H, 7.05; N, 2.51; S, 5.75%);υ_{max}(film)/cm^{-1} 3278 (NH), 1316, 1155 (SO_2) and 1092 br (SiO, CO); δ_H(400MHz, $CDCl_3$) 1.01 (3H, s, CH_3), 1.13 (9H, s, C_4H_9), 2.37 (3H, s, $C_6H_4C\underline{H}_3$), 2.94 (1H, d, *J* 13, one of CH_2), 3.02 (1H, d, *J* 13, one of CH_2), 3.35 (1H, d, *J* 10, one of CH_2OSi), 3.38 (1H, d, *J* 10, one of CH_2OSi), 4.82 (1H, s, $N\underline{H}SO_2C_6H_4$), 7.10-7.19 (7H, m, Ar-H), 7.36-7.46 (6H, m, Ar-H) and 7.58-7.64 (6H, m, Ar-H); *m/z* (CI) 558 (M+H, 1%), 352 (94), 288 (79), 199 (78) and 91 (100).

Table 2, entry 9: Ethylmagnesium chloride (3.5 cm^3 of a 3 mol dm^{-3} solution in diethyl ether, 10.44 mmol) in tetrahydrofuran (30 cm^3) was cooled to 0 C and indole (1.22 g, 10.43 mmol) was added portionwise. The reaction mixture was then heated under reflux for 2 h and allowed to cool to room temperature. The reaction was added dropwise into a cooled (-40 C) solution **(R)-5** (1.00 g, 2.08 mmol) and copper bromide-dimethylsulfide complex (83 mg, 0.2%/mmol) in tetrahydrofuran (30 cm^3). The reaction was allowed to warm to room temperature, heated under reflux for 16 h and quenched with NH_4Cl (sat. aq.) (200 cm^3). The aqueous phase was extracted with ethyl acetate (2 x 200 cm^3). The combined organic phases were washed with brine (200 cm^3), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The residue was chromatographed on silica gel with heptane-ethyl acetate (1:1) as the eluent to yield the regioisomer resulting from C-3 addition as a solid.**(R)-N-[1-(tert-*Butyl-diphenyl-silanyloxymethyl*)-2-(1H-*indol-3-ylmethyl*)-1-*methyl-ethyl*]-4-*methyl-benzenesulphonamide***. (857 mg, 71%), mp 61-62 C (from ethyl acetate); $[\alpha]_D^{18}$ +3.8 (c 1.0 in CH_2Cl_2); (found: C, 70.69; H, 6.72; N, 4.72; S, 5.09. $C_{35}H_{40}N_2O_3SSi$ requires C, 70.43; H, 6.75; N, 4.69; S, 5.37%); υ_{max}(film)/cm^{-1} 3384 (NH), 1427 (C=C), 1317, 1157 (SO_2) and 1090 br (SiO, CO); $^{\delta}{}_H$(400MHz, $CDCl_3$) 1.09 (3H, s, CH_3), 1.12 (9H, s, C_4H_9), 2.37 (3H, s, $C_6H_4C\underline{H}_3$), 3.05 (1H, d, *J* 14, one of Ind-CH_2) 3.19 (1H, d, *J* 14, one of Ind-CH_2), 3.43 (1H, d, *J* 10, one of CH_2OSi), 5.52 (1H, d, *J* 10, one of CH_2OSi), 4.88 (1H, s, $N\underline{H}SO_2C_6H_4$), 6.89 (1H, d, *J* 2, Ind(2)H), 7.04 (1H, m, Ar-H), 7.17 (3H, m, Ar-H), 7.31-7.39 (5H, m, Ar-H), 7.43 (2H, m, Ar-H), 7.55-7.62 (7H, m, Ar-H) and 7.95 (1H, s, Ind-NH); *m/z* (APCI) 597.6 (M+H, 100%).

(R)-1-*Azido*-3-(tert-*butyl-diphenyl-silanyloxy*)-2-*methyl-propan*-2-*ol* (R)-7: This compound was prepared following the procedure described above for (S)-7 using (S)-2-methyl-glycidol (2 g, 22.7 mmol), 4-dimethylaminopyridine (cat.), imidazole

(1.70 g, 25 mmol), *tert*-butyldiphenylsilylchloride (7.10 cm^3, 27.2 mmol) and dichloromethane (60 cm^3). The residual oil was chromatographed on silica gel with heptane-diethyl ether (95:5) as the eluent to yield the title compound as a colourless oil.**(R)-tert-*Butyl*-(2-*methyl*-*oxiranylmethoxy*)-*diphenyl*-*silane***. (7.28 g, 98%), $[\alpha]_D^{20}$ +7.48 (c 1.1 in CH_2Cl_2); (found: C, 73.52; H, 8.01. $C_{20}H_{26}O_2Si$ requires C, 73.57; H, 8.03%); IR and ^{1}H-NMR identical to its enantiomer; *m/z* (CI) 327 (M+H, 2%), 269 (62), 239 (92), 191 (100) and 183 (56).Following the procedure described above for (S)-7 using (R)-*tert*-butyl-(2-methyl-oxiranylmethoxy)-diphenyl-silane (4.93 g, 15.12 mmol), sodium azide (3.93 g, 60.49 mmol), NH_4Cl (3.24 g, 60.49 mmol), methanol (300 cm^3) and water (60 cm^3). The residual oil was chromatographed on silica gel with heptane-diethyl ether (9:1) as the eluent to yield **(R)-7** as a colourless oil. (4.74 g, 85%), $[\ ]_D^{21}$ +17.3 (c 1.2 in CH_2Cl_2); (found: C, 64.98; H, 7.40; N, 11.19. $C_{20}H_{27}N_3O_2Si$ requires C, 65.01; H, 7.36; N, 11.37%); IR and ^{1}H-NMR identical to (S)-7; *m/z* (APCI) 369.5 (M+, 79%), 281.5 (71), 237.3 (78) and 218.4 (100); (found 392.177340. $C_{20}H_{27}N_3O_2S_iNa$ requires 392.177025).

(S)-2-(tert-*Butyl*-*diphenyl*-*silanylmethyl*)-2-*methyl*-1-(*toluene*-4-*sulphonyl*)-*aziridine* (S)-5 :

This compound was prepared following the procedure described above for (R)-5 using (R)-1-Azido-3-(*tert*-butyl-diphenyl-silanyloxy)-2-methyl-propan-2-ol (R)-7 (5 g, 13.55 mmol), triphenylphosphine (3.90 g, 14.90 mmol), triethylamine (3.77 cm^3, 27.10 mmol), *p*-toluenesulphonyl chloride (5.14 g, 27.10 mmol) and tetrahydrofuran (300 cm^3). The residue was chromatographed on silica gel with heptane-diethyl ether (1:1) as the eluent to yield **(S)-5** as a white solid. (3.64 g, 56%), mp 76-78 C (from heptane-diethyl ether); $[\alpha]_D^{26}$ -25.8 (c 1.1 in CH_2Cl_2); (found: C, 67.82; H, 7.00; N, 2.85; S, 6.62. $C_{27}H_{33}NO_3SSi$ requires C, 67.60; H, 6.93; N, 2.92; S, 6.68%); IR and ^{1}H-NMR identical to (R)-5; *m/z* (CI) 480 (M+H, 1%), 344 (100), 324 (20), 309 (66) and 422 (32); (found 502.185333. $C_{27}H_{33}NO_3SSiNa$ requires 502.184814).

***Reaction of* (S)-2-(tert-*Butyl*-*diphenyl*-*silanylmethyl*)-2-*methyl*-1-(*toluene*-4-*sulphonyl*)-*aziridine* (S)-5 *with nucleophiles* :**

Table 3, entry 1: These compounds were prepared following the procedure described above (table 2, entry 1) **(S)-5** (500 mg, 1.04 mmol), HCl gas and diethyl ether (50 cm^3). The residue was chromatographed on silica gel with heptane-ethyl acetate (4:1) as the eluent to yield a mixture of regioisomers resulting from C-3 and C-2 addition as a colourless gum and as a white solid (495 mg, 92%) in a ratio of 1:1.25 respectively.**(R)-N-[1-(tert-*Butyl*-*diphenyl*-*silanyloxymethyl*)-2-*chloro*-1-*methyl*-*ethyl*]-4-*methyl*-*benzene sulphonamide***. (220 mg, 41%), $[\alpha]_D^{19}$ +1.6 (c 0.6 in CH_2Cl_2); (found: C, 62.94; H, 6.64; N, 2.71; Cl, 7.00; S, 6.67. $C_{27}H_{34}NO_3ClSSi$ requires C, 62.83; H, 6.64; N, 2.71; Cl, 6.87; S, 6.21%); IR and ^{1}H-NMR identical to (table 2, entry 1); (found 516.1795. $C_{27}H_{35}NO_3ClSSi$ requires 516.1761).**(R)-N-[3-[tert-*Butyl*-*diphenyl*-*silanyloxy*)-2-*chloro*-2-*methyl*-*propyl*]-4-*methyl*-*benzene sulphonamide***. (275 mg, 51%), mp 97-98 C (from heptane-diethyl ether); $[\alpha]_D^{22}$ -8.9 (c 1 in CH_2Cl_2); (found: C, 63.19; H, 6.66; N, 2.69; Cl, 7.05; S, 6.13. $C_{27}H_{34}NO_3ClSSi$ requires C, 62.83; H, 6.64; N, 2.71; Cl, 6.87; S, 6.21%); IR and ^{1}H-NMR identical to (table 2, entry 1); (found 516.1795. $C_{27}H_{35}NO_3ClSSi$ requires 516.1761).

Table 3, entry 2: This compound was prepared following the procedure described above (table 2, entry 2) **(S)-5** (300 mg, 0.62 mmol) and formic acid (3 cm^3). The residue was chromatographed on silica gel with heptane-ethyl acetate (7:3) as the eluent to yield the regioisomer resulting from C-2 addition as a colourless gum.**(S)-*Formic acid*-2-(tert-*butyl*-*diphenyl*-*silanyloxymethyl*)-1-*methyl*-1-[(*toluene*-4-*sulphonyl amino*)-*methyl*]-*ethyl ester***. (287 mg, 87%), $[\alpha]_D^{24}$ +4.5 (c 1.0 in CH_2Cl_2); (found: C, 64.19; H, 6.64; N, 2.79; S, 6.12. $C_{28}H_{35}NO_5SSi$ requires C, 63.96; H, 6.71; N, 2.66; S, 6.09%); IR and ^{1}H-NMR identical to (table 2, entry 2); (found 543.2350. $C_{28}H_{39}N_2O_5SSi$ requires 543.2351).

Table 3, entry 3: This compound was prepared following the procedure described above (table 2, entry 3) using **(S)-5** (300 mg, 0.62 mmol), benzylalcohol (195 µl, 1.86 mmol), boron trifluoride etherate (60 µl, cat.) and dichloromethane (20 cm^3). The residue was chromatographed on silica gel with heptane-diethyl ether (1:1) as the eluent to yield the regioisomer resulting from C-3 addition as a gum. **(R)-N-[2-*Benzyloxy*-3-(tert-*butyl*-*diphenyl*-*silanyloxy*)-2-*methyl*-*propyl*]-4-*methyl*-*benzene sulfonamide***. (245 mg, 63%), $[\alpha]_D^{20}$ -8.4 (c 0.5 in CH_2Cl_2); (found: C, 69.29; H, 7.26; N, 2.28; S, 5.17. $C_{34}H_{41}NO_4SSi$ requires C, 69.46; H, 7.03; N, 2.38; S, 5.45%); IR and ^{1}H-NMR identical to (table 2, entry 3); *m/z* (APCI) 588.5 (M+H, 100%).

Table 3, entry 4: This compound was prepared following the procedure described above (table 2, entry 4) using **(S)-5** (300 mg, 0.62 mmol), benzylamine (0.341 cm^3, 3.13 mmol) and tetrahydrofuran (20 cm^3). The residue chromatographed on silica gel with heptane-diethyl ether (4:1) as the eluent to yield the regioisomer resulting from C-3 addition as a oil.**(S)-N-[2-*Benzylamino*-1-(tert-*butyl*-*diphenyl*-*silanyloxymethyl*)-1-*methyl*-*ethyl*]-4-*methyl*-*benzenesulphonamide***. (343 mg, 93%), $[\alpha]_D^{19}$ +1.0 (c 1.4 in CH_2Cl_2); (found: C, 69.61; H, 7.19; N, 4.74; S, 5.40. $C_{34}H_{42}N_2O_3SSi$ requires C, 69.59; H, 7.21; N, 4.77; S, 5.46%); IR and ^{1}H-NMR identical to (table 2, entry 4); *m/z* (CI) 587 (M+H, 32%), 312 (72), 199 (49), 120 (64) and 91 (100).

Table 3, entry 5: This compound was prepared following the procedure described above (table 3, entry 6) using **(S)-5** (300 mg, 0.62 mmol), sodium azide (200 mg, 3.13 mmol) and dimethylformamide (10 cm^3). The residue was chromatographed on silica gel with heptane-diethyl ether (9:1) as the eluent to yield the regioisomer resulting from C-3 addition as a gum. **(S)-N-[2-*Azido*-1-(tert-*butyl-diphenyl-silanyloxymethyl*)-1-*methyl-ethyl*]-4-*methyl-benzene suphonamide***. (286 mg, 87%), $[\alpha]_D^{24}$ +14.6 (c 1.4 in CH_2Cl_2); (found: C, 61.89; H, 6.62; N, 10.65; S, 5.86. $C_{27}H_{34}N_4O_3SSi$ requires C, 62.04; H, 6.56; N, 10.72; S, 6.13%); IR and ^{1}H-NMR identical to (table 2, entry 5); *m/z* (CI) 523 (M+H, 1%), 465 (68), 445 (100), 388 (50) and 199 (50).

Table 3, entry 6: This compound was prepared following the procedure described above (table 3, entry 6) using **(S)-5** (300 mg, 0.62 mmol), thiophenol (62 μl, 1.25 mmol) and dimethylformamide (4 cm^3). The residue was chromatographed on silica gel with heptane-ethyl acetate (9:1) as the eluent to yield the regioisomer resulting from C-3 addition as a gum.**(R)-N-[1-(tert-*Butyl-diphenyl-silanyloxymethyl*)-1-*methyl-2-phenylsulphanyl-ethyl*]-4-*methyl-benzenesulphonamide***. (311 mg, 84%), $[\alpha]_D^{19}$ +13.3 (c 1.2 in CH_2Cl_2); (found: C, 67.16; H, 6.65; N, 2.38; S, 10.98. $C_{33}H_{39}NO_3S_2Si$ requires C, 67.19; H, 6.66; N, 2.37; S, 10.87%); IR and ^{1}H-NMR identical to (table 2, entry 6); *m/z* (CI) 590 (M+H, 0.5%), 466 (532), 388 (50), 352 (55) and 341 (100).

Table 3, entry 7: This compound was prepared following the procedure described above (table 2, entry 7) using **(S)-5** (300 mg, 0.62 mmol), isopropylmagnesium chloride (1.56 cm^3 of a 2 mol dm^{-3} solution in diethyl ether, 3.13 mmol), copper bromide-dimethylsulfide complex (15 mg, 0.2%/mmol) and tetrahydrofuran (25 cm^3). The residue was chromatographed on silica gel with heptane-ethyl acetate (9:1) as the eluent to yield the regioisomer resulting from C-3 addition as a gum. **(S)-N-[1-(tert-*Butyl-diphenyl-silanyloxymethyl*)-1-*methyl-2-phenyl-ethyl*]-4-*methyl-benzenesulphonamide***. (232 mg, 71%), $[\alpha]_D^{18}$ -5.7 (c 1.4 in CH_2Cl_2); (found: C, 68.98; H, 8.19; N, 2.40; S, 6.00. $C_{30}H_{41}NO_3SSi$ requires C, 68.79; H, 7.89; N, 2.67; S, 6.12%); IR and ^{1}H-NMR identical to (table 2, entry 7); *m/z* (CI) 524 (M+H, <1%), 353 (100) and 254 (73).

Table 3, entry 8: This compound was prepared following the procedure described above (table 3, entry 8) using **(S)-5** (300 mg, 0.62 mmol), phenylmagnesium bromide (3.13 cm^3 of a 1 mol dm^{-3} solution in diethyl ether, 3.13 mmol), copper bromide-dimethylsulfide complex (15 mg, 0.2%/mmol) and tetrahydrofuran (25 cm^3). The residue was chromatographed on silica gel with heptane-ethyl acetate (9:1) as the eluent to yield the regioisomer resulting from C-3 addition as a white solid. **(S)-N-[1-(tert-*Butyl-diphenyl-silanyloxymethyl*)-1-*methyl-2-phenyl-ethyl*]-4-*methyl-benzenesulphonamide***. (269 mg, 77%), mp 107-110 C (from heptane-diethyl ether); $[\alpha]_D^{20}$ -10.7 (c 1.0 in CH_2Cl_2); (found: C, 71.23; H, 7.06; N, 2.54; S, 5.92. $C_{33}H_{39}NO_3SSi$ requires C, 71.06; H, 7.05; N, 2.51; S, 5.75%); IR and ^{1}H-NMR identical to (table 2, entry 8); (found 558.2500. $C_{33}H_{40}NO_3SSi$ requires 558.2498).

Table 3, entry 9: This compound was prepared following the procedure described above (table 2, entry 9) using **(S)-5** (5 g, 10.43 mmol), ethylmagnesium bromide (17.4 cm^3 of a 3 mol dm^{-3} solution in diethyl ether, 52.19 mmol), indole (6.10 g, 52.19 mmol), copper bromide-dimethylsulfide complex (415 mg, 0.2%/mmol) and tetrahydrofuran (150 cm^3). The residue was chromatographed on silica gel with heptane-ethyl acetate (1:1) as the eluent to yield the regioisomer resulting from C-3 addition as a white solid. **(S)-N-[1-(tert-*butyl-diphenyl-silanyloxymethyl*)-2-(1H-*indol-3-ylmethyl*)-1-*methyl-ethyl*]-4-*methyl-benzenesulphonamide***. (4.69 g, 67%), mp 59-61 C (from ethyl acetate);$[\alpha]_D^{18}$ -4.2 (c 1.0 in CH_2Cl_2); (found: C, 70.69; H, 6.55; N, 4.95; S, 5.24. $C_{35}H_{40}N_2O_3SSi$ requires C, 70.43; H, 6.75; N, 4.69; S, 5.37%); IR and ^{1}H-NMR identical to (table 2, entry 9) ; *m/z* (CI) 597 (M+H, 1.5%), 466 (34), 388 (31) and 130 (100).

(S)-N-(1-Hydroxymethyl-1-methyl-2-phenyl-ethyl)-4-methyl-benzenesulfonamide 10: TBAF (1M in THF) (16 mmol, 16 cm^3) was added to a solution of **(S)-9** (1.81 g, 3.2 mmol) in THF (15 cm^3) and the mixture was stirred for 12 h. The solvent was evaporated and the residue taken-up in ethyl acetate, washed with water, brine and dried ($MgSO_4$). The solvent was evaporated and the residue was chromatographed on silica gel with 2.5% methanol in dichloromethane as the eluent to give the title compound (1.01 g, 98%) as a white solid, m.p. 124-125^{0}C, $[\alpha]_D^{18}$ +1.7 (c 1.0 in CH_2Cl_2); (found: C, 64.03; H, 6.68; N, 4.35. $C_{17}H_{21}NO_3S$ requires C, 63.92; H, 6.62; N, 4.38%); υ_{max}(film)/cm^{-1} 3512, 3276, 1153; δ_H(400MHz, $CDCl_3$) 0.99 (3H, s, CH_3), 2.40 (3H, s, CH_3), 2.51 (1H, t, J 6.4, OH), 2.85 (2H, m, CH_2Ph), 3.44 (1H, dd, J 6.8 and 12.0, C<u>H</u>$_2$OH), 3.54 (1H, dd, J 6.4 and 12, C<u>H</u>$_2$OH), 5.00 (1H, NH, s), 7.17-7.31 (7H, m, ArH), 7.71 (2H, d, J 8.0, ArH).

(S)-2-Methyl-3-phenyl-2-(toluene-4-sulfonylamino)-propionic acid 11: Alcohol **10** (100 mg, 0.31 mmol) in methanol (0.3 cm^3) was added over 1 hr to a mixture of potassium dichromate (93 mg, 0.31 mmol) in concentrated sulfuric acid (0.1 cm^3) and water (0.6 cm^3). After 12 h, the mixture was extracted with ethyl acetate (3 x 4 cm^3), dried ($MgSO_4$) and the solvent evaporated. The crude residue was chromatographed on silica gel with ethyl acetate as the eluent to give the title compound as a colourless oil (64 mg, 62%) $[\alpha]_D^{18}$ -7.4 (c 1.0 in CH_2Cl_2); (found: C, 60.91; H, 5.81; N, 3.80. $C_{17}H_{19}NO_4S$ requires C, 61.24; H, 5.73; N, 4.20%);

υ_{max}(film)/cm^{-1} 3515, 3265, 1716, 1156;δ_H(400MHz, $CDCl_3$) 1.47 (3H, s, CH_3), 2.40 (3H, s, CH_3), 3.07 (1H, d, J 13, CH_2), 3.21 (1H, d, J 13, CH_2), 5.29 (1H, s, NH), 7.22-7.33 (7H, ArH), 7.72 (2H, d, J 8);

(S)-Methyl 2-amino-2-methyl-3-phenylpropioniate 13: The acid **12** (45 mg, 0.13 mmol) in ethyl acetate (1 cm^3) was added dropwise over 1 h to a solution of 32% HBR in HOAc (5 cm^3). The mixture was stirred at room temperature for 12 h, then cooled to 0°C and water (5 cm^3) was added. The aqueous was washed with ethyl acetate (2 x 4 cm^3) and evaporated. The crude HBr salt of α -methylphenylalanine was used in the next step without further purification. Thus, thionyl chloride (0.047 cm^3, 0.65 mmol) was added to an ice-cooled solution of methanol (3 cm^3) and the mixture stirred for 15 minutes. The acid in methanol (1 cm^3) was added dropwise and the mixture allowed to warm-up to room temperature. The mixture was heated to reflux for 12 h. The solvent was evaporated and the crude residue taken up in ethyl acetate and washed with saturated sodium hydrogen carbonate solution, brine and dried ($MgSO_4$). The solvent was evaporated and the residue passed through a small pad of silica with 3.5% methanol in dichloromethane as the eluent to give the title compound (13 mg, 55%), $[\alpha]_D^{20}$ +4.0 (c 1.0 in EtOH),[lit.[18] $[\alpha]_D^{20}$ +4.0 (c 1.0 in EtOH)].

REFERENCES AND NOTES

1. See Burgaud, B. G. M.; Horwell, D. C.; Pritchard, M. C.; Bernad, N.; Martinez, J. *Tetrahedron : Asymmetry* **1995**, 6, 1081 and references cited therein.
2. Horwell, D. C.; Pritchard, M. C.; Raphy, J.; Ratcliffe, G. *Immunopharmacology* **1996**, 33, 68.
3. Horwell, D. C.; Hughes, J.; Hunter, J. C.; Pritchard, M. C.; Richardson, R. S.; Roberts, E.; Woodruff, G. N. *J. Med. Chem.* **1991**, 34, 404.
4. Boden, P.; Eden, J. M.; Hodgson, J.; Horwell, D. C.; Pritchard, M. C.; Raphy, J.; Suman-Chauhan, N. *Bioorg. Med. Chem. Lett.* **1995**, 5, 1773
5. Horwell, D. C.; Ratcliffe, G. S.; Roberts, E. *Bioorg. Med. Chem. Lett.* **1991**, 1, 169.
6. Higginbottom, M.; Kneen, C.; Ratcliffe, G. S. *J. Med. Chem.* **1992**, 35, 1572.
7. For an overview see Williams, R. M. *Synthesis of Optically Active Amino Acids*; Pergamon Press: Oxford, **1989**; Vol. 7 and Heimgartner, H. *Angew. Chem. Int. Ed. Engl.* **1991**, 30, 238.
8. For a recent review see Tanner, D. *Angew. Chem. Int. Ed. Engl.* **1994**, 33, 599.
9. Wipf, P.; Venkatraman, S.; Miller, C. P. *Tetrahedron Lett.* **1995**, 36, 3639.
10. Shao, H.; Zhu, Q.; Goodman, M. *J. Org. Chem.* **1995**, 60, 790.
11. Solomon, M. E.; Lynch, C. L.; Rich, D. H. *Tetrahedron Lett.* **1995**, 36, 4955.
12. Stamm, H.; Assithianakis, P.; Buchholz, B.; Weiβ, R. *Tetrahedron Lett.* **1982**, 23, 5021.
13. Baldwin, J. E.; Spivey, A. C.; Schofield, C. J.; Sweeney, J. B. *Tetrahedron* **1993**, 49, 6309; a) Baldwin, J. E.; Farthing, C. N.; Russell, A. T.; Schofield, C. J.; Spivey, A. C. *Tetrahedron Lett.* **1996**, 37, 3761.
14. Stewart, J. J. P. *J. Computer-Aided Mol. Des.* **1990**, 4, 1.
15. Lin, F-Y.; Bellos, K.; Stamm, H.; Onistschenko, A. *Tetrahedron* **1992**, 48, 2359.
16. Church, N. J.; Young, D. W. *Tetrahedron Lett.* **1995**, 36, 151.
17. a) Legters, J.; Thijs, L.; Zwanenburg, B. *Recl. Trav. Chim. Pays-Bas* **1992**, 111, 1; b) Dauban, P.; Dubois, L.; Tran Huu Dau, M. E.; Dodd, R. H. *J. Org. Chem.* **1995**, 60, 2035.
18. Yoshihiko, I.; Sawamura, M.; Shirakawa, E.; Hayashizaki, K.; Hayashi, T. *Tetrahedron*, **1988**, 44(17), 5253.

(*Received in UK* 2 *August* 1996; *revised* 27 *August* 1996; *accepted* 29 *August* 1996)