Synthesis of hydroxy pyrrolidines and piperidines *via* free-radical cyclisations

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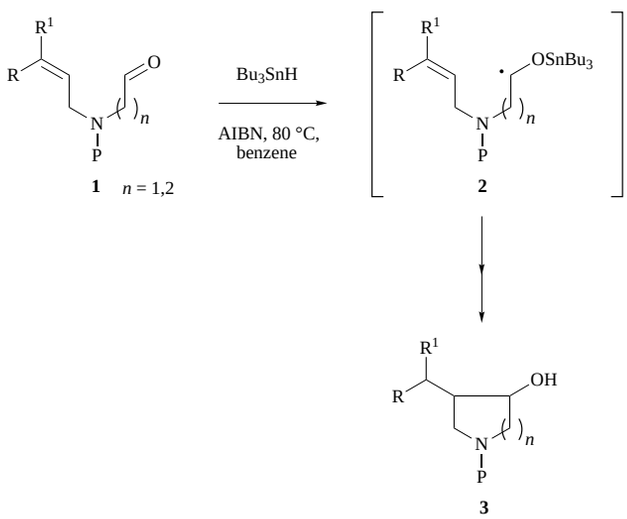
The tin hydride-mediated cyclisation of a variety of α- and β-amino aldehydes to form substituted pyrrolidines and piperidines under mild, neutral reaction conditions has been investigated. The amino aldehyde precursors, prepared from the corresponding amino ester or alcohol, are purified or immediately reacted with Bu_3SnH–AIBN in boiling benzene. The method is shown to be general and cyclisation of the intermediate *O*-stannyl ketyl is observed using a variety of (electron poor or rich) acceptor carbon–carbon double bonds to afford hydroxy-pyrrolidines or -piperidines after work-up. Related cyclisations using an alkyne or α,β-unsaturated amide radical acceptor are shown to be problematic and low-yielding. Radical cyclisation of allylic *O*-stannyl ketyls, generated from reaction of α,β-unsaturated ketones with tin hydride, are also shown to have application in pyrrolidine/piperidine synthesis. A dilution study suggests that the cyclisation onto a cinnamyl double bond is irreversible.

The preparation of hydroxylated pyrrolidines and piperidines has attracted considerable interest in recent years.[1] These are attractive targets because of their widespread occurrence in natural products and the variety of biological activities which they exhibit. Medicinally important examples include lactacystin,[2] oxazolomycin,[3] bulgecinine,[4] deoxynojirimicin,[5] pyrrolizidine alkaloids[6] (such as retronecine) and indolizidine alkaloids (which include castanospermine and pumiliotoxin B).[7] Although tin hydride-mediated radical cyclisation reactions have been widely employed[8] in substituted pyrrolidine/piperidine synthesis the application of this approach to hydroxylated derivatives, starting from carbonyl precursors, has received little attention. Thus while halide, selenide, xanthate and related precursors have been extensively used for many years, it is only recently that the cyclisation of aldehyde and ketone substrates using Bu_3SnH (rather than *e.g.* Na,[9] Zn[10] or Mg[11]) has been adopted.[12] This is surprising as the use of carbonyl precursors not only leads to products which retain a versatile hydroxy group but the tin by-products are more easily removed than, for example, tin chlorides or bromides. Enholm and co-workers[13] first demonstrated the cyclisation of *O*-stannyl ketyls, generated from reaction of tributyltin hydride with aldehydes or ketones, onto electron poor alkenes to produce cycloalkanols. It was found that an activating or electron-withdrawing function on the alkene acceptor was an essential prerequisite for the success of the cyclisation. (It should be noted that related cyclisations have been reported using catalytic Bu_3SnH in the presence of $PhSiH_3$.[14]) In addition to *O*-stannyl ketyls, the cyclisation of allylic *O*-stannyl ketyls, prepared from α,β-unsaturated ketones, to give substituted cycloalkanes is also possible.[15] These studies on carbocyclic systems suggested that related cyclisations could find application in hydroxy pyrrolidine/piperidine synthesis. Hence cyclic amino alcohols have recently been prepared from tin hydride-mediated cyclisation of aldehydes/ketones containing an oxime ether (as radical acceptor)[16] and the pyrrolidine ring present in bulgecinine has been assembled following cyclisation of an *O*-stannyl ketyl onto an $\Delta^{4,5}$-oxazolidinone.[17] We now report[18] the preparation of hydroxy pyrrolidines/piperidines **3** on cyclisation of *N*-protected α- or β-amino aldehydes **1** which contain a variety of carbon–carbon double bond acceptors (Scheme 1). The effect of the radical acceptor and ring size on the yield of cyclisation of the intermediate *O*-stannyl ketyl **2** has been examined and preliminary results centred on the application of *O*-allylic ketyl cyclisations in pyrrolidine/piperidine synthesis are reported.



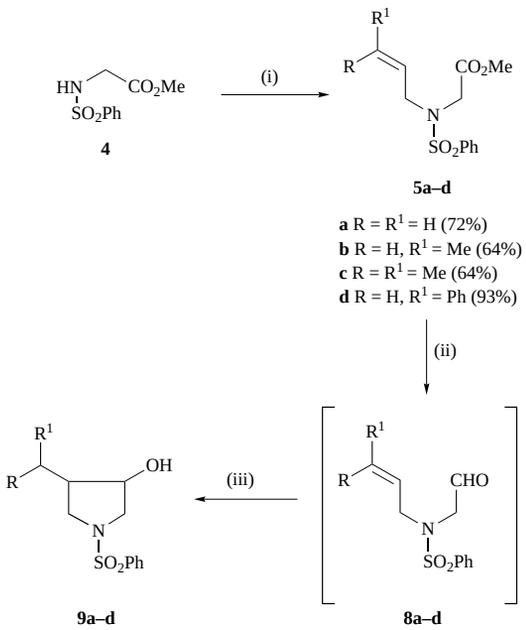
Scheme 1

Initial studies centred on the preparation of aldehyde precursors bearing electron rich alkenes and both a reductive and oxidative approach to these compounds was investigated. Methyl esters **5a–d** were prepared in good yield from the glycine derivative **4** while amino alkanols **6a**,**b** were elaborated to alcohols **7a–d** and the key step in both syntheses involved the *N*-alkylation of secondary sulfonamides (Schemes 2 and 3). The synthesis and subsequent cyclisation of *N*-sulfonyl aldehydes **8a–d** was then explored (Scheme 2, Table 1). Reduction of **5a–d** using DIBAL-H at −78 °C for 1.5 h gave rise to the desired aldehyde cyclisation precursors **8a–d** after work-up and, for example, the formation of **8a** was evident from the ^{1}H NMR spectrum of the crude reaction mixture which showed a singlet corresponding to the aldehydic proton at δ 9.38. Reaction of the crude *N*-allyl derivative **8a** with Bu_3SnH (1.5 equiv.) and AIBN (0.2 equiv.) in boiling benzene (0.1 M) for 2 h gave rise to the desired pyrrolidinol **9a**, as an inseparable 1:1 mixture of diastereoisomers, in 36% overall yield after column chromatography (Table 1, entry 1). A small amount (10%) of methyl ester **5a** starting material was also isolated. Similar yields and diastereoselectivities were observed on reduction and cyclisation of the related aldehydes **8b–d** (Table 1, entries 2–4). In some cases the cyclisation reactions were slow and further AIBN was added until all the starting material had been

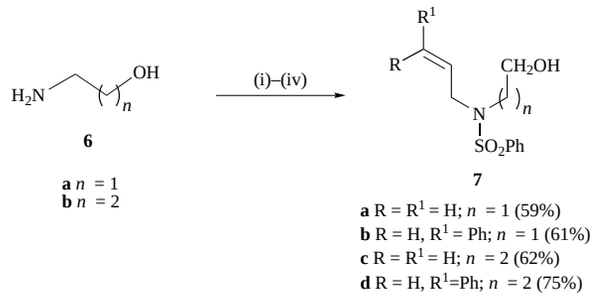
Table 1 Tin mediated radical cyclisations of aldehydes **8a–d**

Entry	Ester **5**	R	R^1	Aldehyde **8**	Yield of **9** (%)	Diastereomer ratio
1	**a**	H	H	**a**	40[a]	1.0:1[b]
2	**b**	H	Me	**b**	50	1.2:1
3	**c**	Me	Me	**c**	42	1.2:1
4	**d**	H	Ph	**d**	52	1.6:1

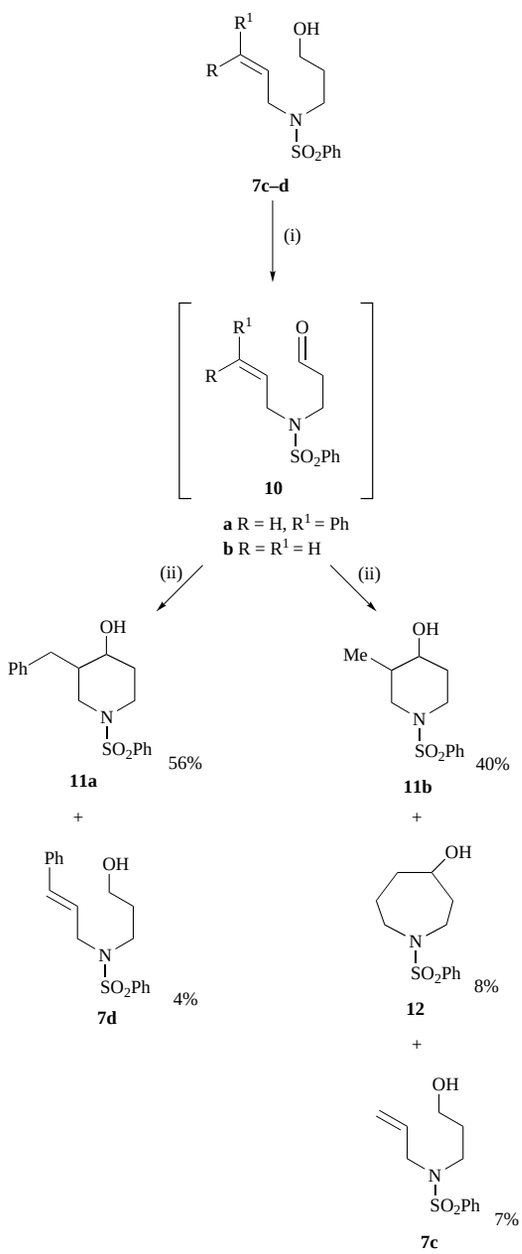
[a] Yield based on recovered ester **5a** (10%). [b] Diastereoisomer ratio determined from the ^{1}H NMR spectrum.



Scheme 2 *Reagents and conditions*: (i) NaH, DMF, 0 °C then $R^1(R)C{=}CHCH_2X$; (ii) DIBAL-H, toluene, −78 °C; (iii) Bu_3SnH, AIBN, benzene, 80 °C (see Table 1)



Scheme 3 *Reagents and conditions*: (i) TBDMSCl, Et_3N, DMAP, CH_2Cl_2; (ii) $PhSO_2Cl$, Et_3N, DMAP, CH_2Cl_2; (iii) NaH, DMF, 0 °C then $R^1(R)C{=}CHCH_2X$; (iv) TsOH, MeOH



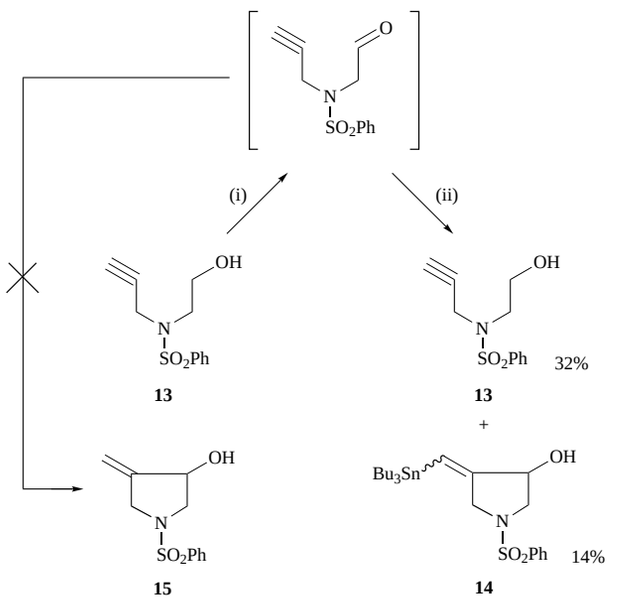
Scheme 4 *Reagents and conditions*: (i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −60 °C; (ii) Bu_3SnH, AIBN, benzene, 80 °C

consumed. Attempted cyclisation of **8d** at higher temperature in boiling toluene, rather than benzene, was less successful and the yield of pyrrolidinol **9d** dropped from 52 to 17%.

The preparation and subsequent cyclisation of aldehyde **8d**, derived from oxidation of alcohol **7b**, was also explored. Initial reactions using TPAP, PCC or PDC as the oxidising agent proved unsuccessful but Swern oxidation at −60 °C was found to be an efficient and clean method for the preparation of **8d**. Treatment of the crude oxidation product with Bu_3SnH resulted in the formation of the pyrrolidinol **9d** in identical yield (52%) and diastereoselectivity (1.6:1) to that obtained earlier starting from methyl ester **5d**. This approach could also be extended to piperidinol synthesis and oxidation of the primary alcohol **7d** to **10a** followed by reaction with Bu_3SnH (added over 3 h) gave rise to the desired secondary alcohol **11a** in 56% yield after column chromatography (Scheme 4). This resulted from a 6-*exo-trig* cyclisation process and the stereochemistry of the two separable diastereoisomers, isolated in a ratio of 1.3:1, was not deduced. In addition to **11a** a small amount of the primary alcohol **7d**, derived from simple reduction of the intermediate aldehyde, was also formed. The ^{1}H NMR spectrum of the oxidation reaction showed clean aldehyde formation and so the isolation of **7d** was attributed to the Bu_3SnH reaction rather than recovery of unreacted starting material. Reaction of the *N*-allyl derivative **7c**, under the same conditions, afforded piperidinol **11b** in 40% yield and alcohol **7c** (derived from reduction of aldehyde **10b**) in 7% yield. In addition, the azepane **12** was formed in 8% yield and this presumably arises from a competitive 7-*endo* cyclisation of the intermediate *O*-stannyl ketyl radical. These results contrast

with the previously reported hept-6-enyl-1-oxy cyclisations.[13] In this case 6-*exo* cyclisation, to form a cyclohexanol, was only possible when an activated alkene was present. The introduction of an ester substituent on the alkene (which lowered the energy of the LUMO) was shown to result in a bonding interaction with the (high energy) SOMO of the electron-rich *O*-stannyl ketyl radical. Clearly alkene activation (with an electron-withdrawing group) is not essential for the cyclisations reported here and this highlights the importance of the amino linkage in facilitating this type of reaction.

The cyclisation of a precursor bearing an alkyne as the radical acceptor was also undertaken as shown in Scheme 5.



Scheme 5 *Reagents and conditions*: (i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −60 °C; (ii) Bu_3SnH, AIBN, benzene, 80 °C

The *N*-prop-2-ynyl sulfonamide **13**, prepared from the protected glycine **4**, was oxidised and subjected to radical cyclisation conditions. However, the major product after purification was the primary alcohol **13** derived from simple reduction of the intermediate aldehyde. The minor product, isolated in 14% yield, was characterised as stannane **14** which was thought to result from addition of the tributyltin radical to the alkyne followed by 5-*exo* cyclisation onto the aldehyde carbonyl.[19] None of the expected 4-*exo*-methylene pyrrolidine **15** was evident and this may reflect the nucleophilic nature of the intermediate *O*-stannyl ketyl radical which results in no interaction with the electron rich C≡C triple bond (and consequently no cyclisation).

An alternative strategy was employed for the preparation of aldehyde precursors bearing electron deficient double bonds. This involved oxidative cleavage of the alkene present in **7a** using ozone at −78 °C to give lactol **16**, as a stable white solid, in 90% yield (Scheme 6). The ^1H NMR spectrum of **16** in $CDCl_3$ showed the absence of any open chain hydroxy aldehyde in accord with that observed for related compounds.[20] Similar oxidation of the propanol derivative **7c** gave **17** which surprisingly existed entirely as the 7-membered ring lactol (from the ^1H NMR spectrum). Wittig reaction of **16** with ethyl (triphenylphosphoranylidene)ethanoate in CH_2Cl_2 at 40 °C for 12 h followed by careful column chromatography afforded pure samples of the *cis*- and *trans*-unsaturated esters, **18a** and **18b**, in 30 and 31% yield respectively. Reaction of related hemiacetals[21] with stabilised phosphoranes have also given rise to high levels of the *cis*-alkene isomer and a similar alkene *Z*:*E* ratio was observed on reaction of lactol **17** to afford **18c**,**d**.

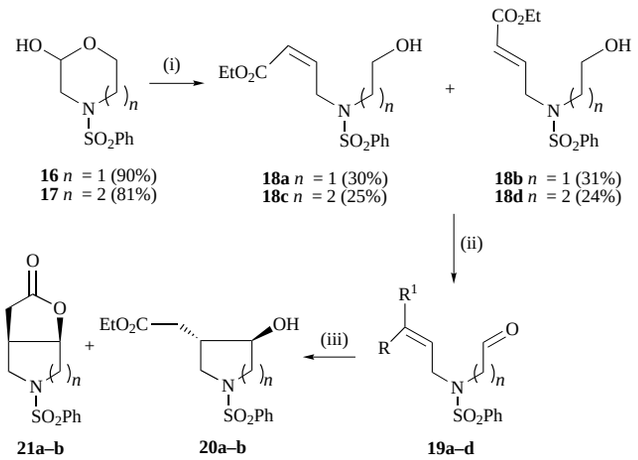
Swern oxidation of the *cis*-alkene **18a** and purification using column chromatography afforded pure aldehyde **19a** in 65% yield. Cyclisation of this aldehyde resulted in the formation of the desired *trans*-pyrrolidine **20a** and *cis*-bicycle **21a** in 27 and 29% yield respectively (Table 2, entry 1). Both products resulted from an initial 5-*exo* radical cyclisation and the bicycle **21a** was thought to arise from a second cyclisation involving attack of the tin alkoxide onto the ester. Considerably lower yields of **20a** and **21a** were isolated when cyclisation of the crude aldehyde **19a** was attempted. The cyclisation of aldehyde **19b** (derived from alcohol **18b**) bearing a *trans*-alkene produced **20a** and **21a** in similar yields and so the precursor double bond stereochemistry was shown to have little effect on the diastereoselectivity of the cyclisation reaction (Table 2, entry 2). This method was also applied to piperidine synthesis and similar yields of 6-*exo* cyclisation, to produce **20b** and **21b**, were obtained starting from aldehydes **19c**,**d** which in turn were derived from the corresponding alcohols **18c**,**d** (Table 2, entries 3 and 4). It should be noted that no primary alcohol resulting from simple reduction of aldehyde **19a**–**d** was isolated from these reactions. Lactol **16** could alternatively be reacted with phosphorane **22**, derived from α-bromo-γ-butyrolactone, to afford trisubstituted alkene **23** (as the *trans*-isomer), which unfortunately could not be separated from triphenylphosphine oxide even after extensive column chromatography (Scheme 7). However, a pure sample of **23** could be obtained from chromatography of the corresponding (and more nonpolar) *O*-silyl ether followed by acid desilylation. Cyclisation of the crude aldehyde prepared on oxidation of **23** was also successful and secondary alcohol **24** was isolated as a mixture of three diastereoisomers (in a ratio of 1.3:1.3:1) in 48% yield over the two steps. A small amount (6%) of the secondary sulfonamide **25** (which may result from β-elimination of the intermediate *O*-stannyl ketyl radical) was also isolated.

It was also envisaged that substituted pyrrolidinones could be prepared by radical cyclisation onto an electron poor unsaturated amide double bond. In order to investigate this approach the *N*-benzyl cinnamide **26** was prepared starting from *N*-benzyl glycine methyl ester (Scheme 8). Oxidation and subsequent treatment of the crude aldehyde with Bu_3SnH resulted in a slow

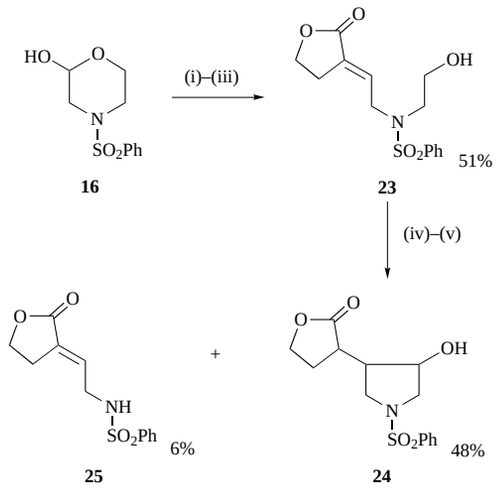
Table 2 Tin mediated radical cyclisations of aldehydes **19a**–**d**

Entry	Aldehyde **19**	R	R^1	*n*	Products [yield (%)]
1	**a**	CO_2Et	H	1	**20a** (27) + **21a** (29)
2	**b**	H	CO_2Et	1	**20a** (33) + **21a** (32)
3	**c**	CO_2Et	H	2	**20b** (23) + **21b** (25)[a]
4	**d**	H	CO_2Et	2	**20b** (29) + **21b** (27)

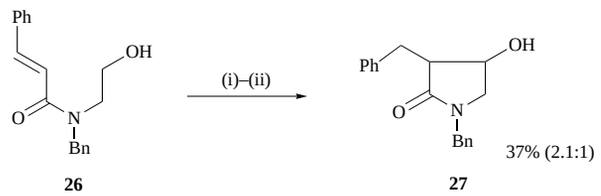
[a] Crude aldehyde **19c** was used and the yield is based on precursor alcohol **18c**.



Scheme 6 *Reagents and conditions*: (i) $Ph_3P{=}CHCO_2Et$, CH_2Cl_2, 40 °C; (ii) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −60 °C; (iii) Bu_3SnH, AIBN, benzene, 80 °C (see Table 2)



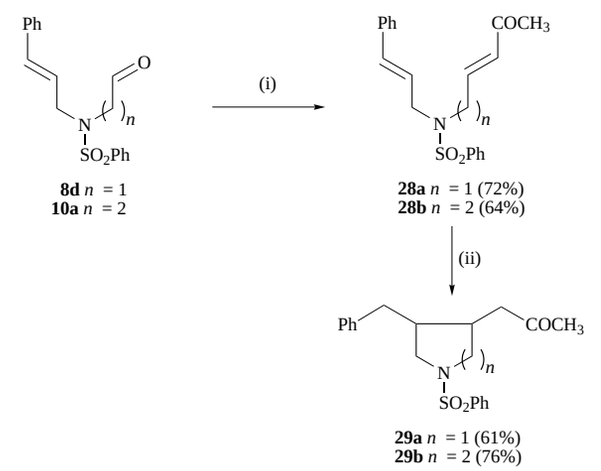
Scheme 7 *Reagents and conditions*: (i) 3-triphenylphosphoranylidene-2-oxotetrahydrofuran **22**, CH_2Cl_2, 40 °C; (ii) TBDMSCl, Et_3N, DMAP, CH_2Cl_2; (iii) TsOH, MeOH; (iv) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −60 °C; (v) Bu_3SnH, AIBN, benzene, 80 °C



Scheme 8 *Reagents and conditions*: (i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −60 °C; (ii) Bu_3SnH, AIBN, benzene, 80 °C

conversion to the desired pyrrolidinone **27** as a 2.1 : 1 mixture of inseparable diastereoisomers. However, only a modest unoptimised yield of 37% was obtained for this reaction even though no starting material or any by-products could be isolated.

Finally, the application of allylic *O*-stannyl ketyls in pyrrolidine/piperidine synthesis was briefly explored. In this case an unsaturated ketone would act as a free-radical precursor rather than an acceptor as commonly employed in 1,4-addition reactions. The precursor dienes **28a**,**b** were prepared in good yield from Wittig reaction of aldehydes **8d** and **10a** using an excess (5 equiv.) of (triphenylphosphoranylidene)propan-2-one (Scheme 9). Treatment of these dienes with Bu_3SnH (0.1 M in benzene)



Scheme 9 *Reagents and conditions*: (i) $Ph_3P{=}CHCOCH_3$, CH_2Cl_2; (ii) Bu_3SnH, AIBN, benzene, 80 °C

resulted in clean cyclisation and the desired disubstituted *N*-heterocycles **29a** and **29b** were isolated in 61 and 76% yield respectively. Both products were isolated as diastereomeric mixtures, in the ratio 2.6–1.5 : 1, which were not separable on column chromatography. Related work[15] has established that very high levels of diastereoselectivity (>50 : 1) can be obtained when the concentration of reactants is reduced from 0.1 to 0.01 M. These observations have been attributed to the reversibility of the cyclisation and the decreased availability of the Bu_3SnH. However, when the cyclisation of **28b** was carried out under dilute conditions (0.01 M) the piperidine **29b** was produced in similar yield (71%) and diastereoselectivity (2.6 : 1) to that obtained earlier. This suggested that cyclisation of the allylic *O*-stannyl ketyl radical onto the styrene double bond was irreversible.

This work has demonstrated the radical cyclisation of a range of α- and β-amino aldehydes containing a variety of double bonds. The method is general and both electron rich and poor alkenes can be utilised to afford substituted pyrrolidines or piperidines. No products derived from hydrostannylation of the alkene precursors were isolated but this reaction did prove problematic when an alkyne radical acceptor was used. The application of allylic *O*-stannyl ketyl cyclisations in *N*-heterocycle synthesis has also been demonstrated for the first time and future work will concentrate on the use of this method in natural product synthesis.

Experimental

IR spectra were recorded on an ATI Mattison Genesis FT IR spectrometer. ^1H and ^{13}C NMR spectra were recorded on a JEOL EX 270 spectrometer; the carbon spectra were assigned using DEPT experiments. Coupling constants (J) were recorded in Hz to the nearest 0.5 Hz. Mass spectra were recorded on a Fisons Instruments VG Analytical Autospec Spectrometer system. Thin layer chromatography (TLC) was performed on Merck aluminium-backed silica gel plates. Compounds were visualised under a UV lamp, using basic $KMnO_4$ solution, ninhydrin and/or iodine. Column chromatography was performed using silica gel (Matrix Silica 60, 70–200 micron Fisons or ICN flash silica 60, 32–63 microns). Solvents were purified/dried using standard literature methods. Light petroleum refers to the fraction with bp 40–60 °C. Bu_3SnH was purchased from Lancaster Synthesis Ltd and distilled before use. Elemental analyses were performed by the Chemical Analytical Services Unit, University of Newcastle.

General procedure for the alkylation of sulfonamide 4

To a stirred solution of sulfonamide **4** (1.38–5.27 mmol) in anhydrous DMF (5–10 cm^3) was added NaH (1.66–6.32 mmol) under a nitrogen atmosphere. After stirring for 0.2 h at room temperature the mixture was cooled to 0 °C and a solution of the halide (2.07–7.91 mmol) in anhydrous DMF (1 cm^3) was added gradually *via* a syringe. The reaction was then allowed to warm to room temperature and stirred until the starting material had been consumed as shown by TLC (2–10 h). EtOAc (20 cm^3) and water (20 cm^3) were added and the mixture was stirred vigorously for 0.5 h. The organic layer was separated, washed with more water (2 × 20 cm^3) and brine (20 cm^3), dried ($MgSO_4$), concentrated and purified by column chromatography (silica; light petroleum–Et_2O) to afford **5a**–**d** (64–93%) as a colourless oil or a white crystalline solid.

Methyl (*N*-allyl-*N*-phenylsulfonylamino)ethanoate 5a. R_f 0.4 (petroleum ether–Et_2O, 1 : 1); ν_{max}(thin film)/cm^{-1} 1753 (s), 1446 (m), 1419 (w), 13 743 (s), 1214 (m), 1162 (s), 1092 (m); δ_H(270 MHz, $CDCl_3$) 7.96–7.44 (5H, m, aromatics), 5.85–5.70 (1H, m, $CH_2{=}CH$), 5.30–5.23 (2H, app. t, J 9, $CH_2{=}CH$), 4.12 (2H, s, NCH_2CO), 4.00 (2H, d, J 6.5, NCH_2CH), 3.70 (3H, s, CO_2Me); δ_C(67.5 MHz, $CDCl_3$) 169.2 (CO_2Me), 139.7 ($C{=}CH$), 132.7 ($CH_2{=}CH$), 132.0, 129.0, 127.2 ($CH{=}C$), 119.9 ($CH_2{=}CH$), 52.0 (CO_2Me), 50.7, 46.7 (2 × NCH_2); *m*/*z* (CI, NH_3) 287 ($M + NH_4^+$, 100%), 270 ($M + H^+$, 51), 210 (18), 200 (6), 128 (52) (Found: $M + H^+$, 270.0799. $C_{12}H_{15}NO_4S$ requires $M + H^+$, 270.0800).

Methyl (*N*-phenylsulfonyl-*N*-but-2-enylamino)ethanoate 5b. R_f 0.5 (light petroleum–Et_2O, 1:1); ν_{max}(thin film)/cm^{-1} 1752 (s), 1445 (m), 1341 (m), 1161 (s), 970 (w), 925 (w); δ_H(270 MHz, $CDCl_3$) 7.88–7.48 (5H, m, aromatics), 5.64–5.52 (1H, m, MeC*H*=C), 5.45–5.24 (1H, m, MeCH=C*H*), 4.02 (2H, s, NCH_2CO), 3.83 (2H, d, *J* 7, NCH_2CH), 3.61 (3H, s, CO_2Me), 1.65 (3H, dd, *J* 6 and 1.5, *Me*CH=C); δ_C(67.5 MHz, $CDCl_3$) 169.4 (*C*O_2Me), 139.9 (*C*=CH), 132.6, 131.9, 128.9, 127.3 (*C*H=C and MeCH=C), 123.6 (MeCH=*C*H), 52.1 (CO_2Me), 50.1, 46.6 (2 × N*C*H_2), 17.7 (*Me*CH=C); *m*/*z* (CI, NH_3) 301 (M + NH_4^+, 16%), 284 (M + H^+, 41), 247 (24), 214 (22), 142 (43), 83 (70), 49 (100) (Found: M + H^+, 284.0953. $C_{13}H_{17}NO_4S$ requires *M* + H^+, 284.0957).

Methyl (*N*-phenylsulfonyl-*N*-3-methylbut-2-enylamino)ethanoate 5c. R_f 0.5 (light petroleum–Et_2O, 1:1); ν_{max}(thin film)/cm^{-1} 3060 (m), 2986 (m), 2943 (m), 2919 (m), 1745 (s), 1145 (s), 1338 (s), 1309 (m), 1217 (m), 1158 (s), 1097 (m), 1073 (m); δ_H(270 MHz, $CDCl_3$) 7.91–7.52 (5H, m, aromatics), 5.07 (1H, t, *J* 7.5, C=C*H*CH$_2$), 4.05 (2H, s, NCH_2CO), 3.96 (2H, d, *J* 7.5, NCH_2CH), 3.65 (3H, s, CO_2Me), 1.72, 1.60 (6H, 2 × s, Me_2C=CH); δ_C(67.5 MHz, $CDCl_3$) 169.3 (*C*O_2Me), 139.7, 139.0 (*C*=CH, Me*C*=CH), 132.4, 128.7, 127.0 (*C*H=C), 117.6 (Me_2C=*C*H), 51.8 (CO_2Me), 46.3, 45.1 (2 × N*C*H_2), 25.5, 17.4 (Me_2C=CH); *m*/*z* (CI, NH_3) 315 (M + NH_4^+, 69%), 298 (13), 247 (100), 228 (26), 156 (96) (Found: M + NH_4^+, 315.1377. $C_{14}H_{19}NO_4S$ requires *M* + NH_4^+, 315.1379).

Methyl (*N*-phenylsulfonyl-*N*-cinnamylamino)ethanoate 5d. Mp 69–71 °C; R_f 0.4 (light petroleum–Et_2O, 2:1); ν_{max}(thin film)/cm^{-1} 1756 (s), 1146 (s), 1340 (s), 1206 (m), 1161 (m), 918 (m), 750 (m), 693 (m); δ_H(270 MHz, $CDCl_3$) 7.82–7.16 (10H, m, aromatics), 6.38 (1H, d, *J* 16, PhC*H*=CH), 5.95 (1H, dt, *J* 16 and 7, PhCH=C*H*), 4.00–3.99 (4H, m, 2 × NCH_2), 3.51 (3H, s, CO_2Me); δ_C(67.5 MHz, $CDCl_3$) 169.3 (*C*O_2Me), 139.7, 135.8 (*C*=CH), 134.8 (Ph*C*H=CH), 132.7, 128.9, 128.6, 128.1, 127.3, 126.5 (*C*H=C), 123.0 (PhCH=*C*H), 52.1 (CO_2Me), 50.4, 46.9 (2 × N*C*H_2); *m*/*z* (CI, NH_3) 363 (M + NH_4^+, 8%), 346 (M + H^+, 1), 247 (54), 204 (49), 117 (100) (Found: M + NH_4^+, 363.1377. $C_{18}H_{19}NO_4S$ requires *M* + NH_4^+, 363.1379).

General procedure for the preparation of sulfonamides 7a–d

To a solution of amino alcohol **6a**–**b** (13.3–65.6 mmol) in dry CH_2Cl_2 (50–100 cm^3) was added Et_3N (14.6–72.1 mmol), TBDMSCl (14.6–72.1 mmol) and a catalytic quantity of DMAP. The reaction was then allowed to stir at room temperature for 12 h. Water (100 cm^3) was added, the mixture was stirred vigorously for 0.1 h and the organic layer was separated, washed with more water (50 cm^3), brine (50 cm^3), dried ($MgSO_4$) and evaporated *in vacuo* to afford crude silylated alcohol which was dissolved in CH_2Cl_2 (10–100 cm^3) and cooled to 0 °C. Et_3N (14.6–72.1 mmol) followed by $PhSO_2Cl$ (14.6–72.1 mmol) [dissolved in CH_2Cl_2 (5–10 cm^3)] was then added gradually over 0.1 h and the reaction allowed to warm to room temperature and stirred for 1 h. The solvent was then removed *in vacuo* and the residue dissolved in EtOAc, washed with water, brine, dried ($MgSO_4$) and evaporated *in vacuo* to afford an oil. Column chromatography (silica) afforded the desired protected amino alcohols (82–85%) as colourless oils. The sulfonamide was then *N*-alkylated using the same method as described earlier for the preparation of **5a**–**d** and the resultant silyl protected alcohol (0.67–1.37 mmol) was dissolved in MeOH (10–20 cm^3), containing a catalytic quantity of *p*-TsOH. The solution was allowed to stir overnight at room temperature and evaporation of the solvent *in vacuo* followed by column chromatography (silica; Et_2O or Et_2O–light petroleum) afforded alcohol **7a**–**d** (72–88%) as a colourless oil.

2-(*N*-Allyl-*N*-phenylsulfonylamino)ethanol 7a. R_f 0.4 (Et_2O); ν_{max}(thin film)/cm^{-1} 3400–3357 (br, m), 1148 (w), 1372 (m), 1347 (m), 1159 (s), 1089 (s); δ_H(270 MHz, $CDCl_3$) 7.87–7.50 (5H, m, aromatics), 5.65 (1H, ddt, *J* 17, 10 and 6.5, CH_2=C*H*), 5.23–5.14 (2H, m, CH_2=CH), 3.87 (2H, d, *J* 6.5, NCH_2CH), 3.74 (2H, t, *J* 5.5, CH_2O), 3.27 (2H, t, *J* 5.5, NCH_2CH$_2$), 2.35 (1H, br s, CH$_2$O*H*); δ_C(67.5 MHz, $CDCl_3$) 139.2 (*C*=CH), 132.7, 129.2, 128.2, 127.1 (*C*H=C and CH_2=*C*H), 119.3 (*C*H_2=C), 60.8 (*C*H_2O), 52.0, 49.6 (2 × N*C*H_2); *m*/*z* (CI, NH_3) 259 (M + NH_4^+, 53%), 242 (M + H^+, 67), 210 (10), 160 (12), 102 (100) (Found: M + H^+, 242.0845. $C_{11}H_{15}NO_3S$ requires *M* + H^+, 242.0851).

2-(*N*-Phenylsulfonyl-*N*-cinnamylamino)ethanol 7b. R_f 0.3 (Et_2O–light petroleum, 3:1); ν_{max}(thin film)/cm^{-1} 3515 (s), 3060 (w), 3031 (w), 2936 (m), 1147 (m), 1333 (s), 1159 (s); δ_H(270 MHz, $CDCl_3$) 8.00–7.31 (10H, m, aromatics), 6.56 (1H, d, *J* 16, PhC*H*), 6.11 (1H, dt, *J* 16 and 7, PhCH=C*H*), 4.15 (2H, d, *J* 7, NCH_2CH), 3.86 (2H, t, *J* 5, CH_2O), 3.42 (2H, t, *J* 5, NCH_2-CH$_2$), 2.25 (1H, s, CH$_2$O*H*); δ_C(67.5 MHz, $CDCl_3$) 139.4, 135.9 (*C*=CH), 134.3 (Ph*C*H=C), 132.8, 129.2, 128.6, 128.1, 127.2, 126.4 (*C*H=C), 123.6 (PhCH=*C*H), 61.1 (*C*H_2O), 51.6, 49.7 (2 × N*C*H_2); *m*/*z* (CI, NH_3) 335 (M + NH_4^+, 20%), 318 (M + H^+, 16), 219 (46), 202 (24), 176 (56), 117 (100) (Found: M + H^+, 318.1175. $C_{17}H_{19}NO_3S$ requires *M* + H^+, 318.1164).

3-(*N*-Allyl-*N*-phenylsulfonylamino)propanol 7c. R_f 0.5 (Et_2O); ν_{max}(thin film)/cm^{-1} 3520–3402 (br, s), 2937 (m), 2879 (m), 1446 (w), 1334 (s), 1159 (s); δ_H(270 MHz, $CDCl_3$) 7.94–7.56 (5H, m, aromatics), 5.70 (1H, ddt, *J* 17, 10 and 6.5, CH_2=C*H*), 5.29–5.20 (2H, m, CH_2=C), 3.93 (2H, d, *J* 6.5, NCH_2CH), 3.83 (2H, t, *J* 6, CH_2O), 3.37 (2H, t, *J* 6, NCH_2CH$_2$), 2.26 (1H, br s, CH$_2$O*H*), 1.83 (2H, quintet, *J* 6, CH$_2$CH_2CH$_2$); δ_C(67.5 MHz, $CDCl_3$) 140.1 (*C*=CH), 133.3, 133.1, 129.6, 127.5 (*C*H=C and CH_2=*C*H), 119.7 (*C*H_2=C), 59.1 (*C*H_2O), 51.5 (N*C*H$_2$CH), 44.3 (N*C*H$_2$CH$_2$), 31.1 (CH$_2$*C*H$_2$CH$_2$); *m*/*z* (CI, NH_3) 273 (M + NH_4^+, 17), 256 (M + H^+, 100), 210 (9), 114 (40) (Found: M + H^+, 256.1000. $C_{12}H_{17}NO_3S$ requires *M* + H^+, 256.1007).

3-(*N*-Phenylsulfonyl-*N*-cinnamylamino)propanol 7d. R_f 0.4 (Et_2O); ν_{max}(thin film)/cm^{-1} 3291 (s), 3051 (m), 3029 (s), 2930 (m), 1450 (s), 1341 (m), 1152 (s); δ_H(270 MHz, $CDCl_3$) 7.98–7.31 (10H, m, aromatics), 6.54 (1H, d, *J* 16, PhC*H*=C), 6.06 (1H, dt, *J* 16 and 7, PhCH=C*H*), 4.10 (2H, d, *J* 7, NCH_2-CH=C), 3.85 (2H, t, *J* 6, CH_2O), 3.43 (2H, t, *J* 6, NCH_2CH$_2$), 2.32 (1H, br s, CH$_2$O*H*), 1.85 (2H, quintet, *J* 6, CH$_2$CH_2CH$_2$); δ_C(67.5 MHz, $CDCl_3$) 139.7, 135.7 (*C*=CH), 134.1 (Ph*C*H=CH), 132.6, 129.2, 128.6, 128.0, 127.1, 126.4 (*C*H=C), 123.6 (PhCH=*C*H), 58.7 (*C*H_2O), 50.5, 43.9 (2 × N*C*H_2), 30.8 (CH$_2$*C*H$_2$CH$_2$); *m*/*z* (CI, NH_3) 349 (M + NH_4^+, 20%), 332 (M + H^+, 70), 233 (35), 216 (19), 190 (43), 134 (32), 117 (100) (Found: M + H^+, 332.1322. $C_{18}H_{21}NO_3S$ requires *M* + H^+, 332.1320).

General procedure for the synthesis and cyclisation of α-amino aldehydes 8a–d

To a solution of methyl ester **5a**–**d** (0.54–0.81 mmol) in dry toluene (10–100 cm^3) was added DIBAL-H (1 M solution in hexanes, 0.92–1.38 mmol) dropwise while stirring at −78 °C under a nitrogen atmosphere. After 1.5 h MeOH (1–2 cm^3) was added dropwise to quench the reaction, followed by 10% aqueous citric acid (20–50 cm^3) to solubilise the complex. The mixture was allowed to warm to room temperature and stirred for 1 h. EtOAc (20 cm^3) was added and the organic layer was separated, washed with brine, dried ($MgSO_4$) and evaporated *in vacuo* to afford the crude amino aldehyde **8a**–**d** as a clear oil. This was immediately dissolved in degassed benzene (5–8 cm^3) and Bu_3SnH (0.81–1.22 mmol) and AIBN (0.10–0.16 mmol) were added in degassed benzene (0.5 cm^3) under a nitrogen atmosphere. The reaction mixture was then heated at reflux until starting material was consumed as indicated by TLC (2–12 h) [additional portions of AIBN (0.1 mmol) were added at 2 h intervals]. The reaction mixture was then concentrated *in vacuo* and the crude product was separated by flash column chromatography (silica; Et_2O–light petroleum) to afford pyrroldinol **9a**–**d** (36–52%) as a colourless oil or a white solid.

1-Phenylsulfonyl-4-methylpyrrolidin-3-ol 9a. R_f 0.2 (Et_2O–light petroleum, 3:1); ν_{max}(thin film)/cm^{-1} 3514 (br, s), 1472 (w), 1447 (m), 1333 (s), 1219 (m), 1162 (s), 1094 (s), 1074 (m), 1054

(m); δ_H(270 MHz, $CDCl_3$) (two diastereomers) 7.93–7.58 (5H, m, aromatics), 4.20 and 3.93 (1H, 2 × br m, C*H*OH), 3.64–3.53 (2H, m, 2 × NC*H*), 3.43 (1H, dd, *J* 11.5 and 1.46, NC*H*), 3.26 (1H, dd, *J* 10.5 and 3.5, NC*H*), 2.17–2.12 (1H, m, MeC*H*), 1.95 (1H, br s, CHO*H*), 1.06 and 0.94 (3H, d, *J* 7, *Me*CH); δ_C(67.5 MHz, $CDCl_3$) (2 diastereomers) 137.4, 137.0 (*C*=CH), 133.1, 129.5, 127.8 (*C*H=C), 76.7, 66.3 (*C*HOH), 56.8, 54.6, 53.1, 52.3 (2 × NCH_2), 41.4, 38.9 (Me*C*H), 15.7, 11.2 (*Me*CH); *m*/*z* (CI, NH_3) 259 (M + NH_4^+, 23%), 242 (M + NH_4^+, 100), 100 (26) (Found: M + H^+, 242.0849. $C_{11}H_{15}NO_3S$ requires *M* + H^+, 242.0851).

1-Phenylsulfonyl-4-ethylpyrrolidin-3-ol 9b. *Major diastereoisomer*; R_f 0.4 (Et_2O–light petroleum, 4:1); ν_{max}(thin film)/cm^{-1} 3515 (br, s), 1446 (m), 1332 (s), 1163 (s), 1094 (m); δ_H(270 MHz, $CDCl_3$) 7.78–7.42 (5H, m, aromatics), 4.13 (1H, t, *J* 3.5, C*H*OH), 3.44 (1H, app. t, *J* 9, NC*H*), 3.36–3.33 (2H, m, 2 × NC*H*), 2.91 (1H, app. t, *J* 10, NC*H*), 1.97–1.16 (4H, m, MeCH_2, MeCH_2C*H* and CHO*H*), 0.93 (3H, t, *J* 7.5, *Me*CH_2); δ_C(67.5 MHz, $CDCl_3$) 137.0 (*C*=CH), 132.7, 129.1, 127.2 (*C*H=C), 71.3 (*C*HOH), 56.7, 50.4 (2 × N*C*H_2), 48.0 (MeCH_2-*C*H), 26.5 (Me*C*H_2), 12.0 (*Me*CH_2); *m*/*z* (CI, NH_3) 255 (M + H^+, 11%), 224 (5), 170 (13), 141 (100), 114 (75) (Found: M + H^+, 255.0927. $C_{12}H_{17}NO_3S$ requires *M* + H^+, 255.0929). *Minor diastereoisomer*; R_f 0.37 (Et_2O–light petroleum, 4:1); ν_{max}(thin film)/cm^{-1} 3515 (br, m), 1462 (m), 1446 (m), 1333 (s), 1162 (s), 1094 (m); δ_H(270 MHz, $CDCl_3$) 7.79–7.43 (5H, m, aromatics), 3.91–3.86 (1H, m, C*H*OH), 3.47–3.33 (2H, m, 2 × NC*H*), 3.10 (1H, dd, *J* 10.5 and 4, NC*H*), 2.94 (1H, dd, *J* 10.5 and 5.5, NC*H*), 1.87–1.75 (2H, m, MeCH_2), 1.10–0.83 (2H, m, MeCH_2C*H* and CHO*H*), 0.79 (3H, t, *J* 7.5, *Me*CH_2); δ_C(67.5 MHz, $CDCl_3$) 136.4 (*C*=CH), 132.8, 129.3, 127.4 (*C*H=C), 75.0 (*C*HOH), 54.5, 50.9 (2 × N*C*H_2), 48.3 (MeCH_2*C*H), 24.1 (Me*C*H_2), 12.0 (*Me*CH_2); *m*/*z* (CI, NH_3) 255 (M + H^+, 10%), 170 (7), 114 (65), 77 (64), 42 (100) (Found: M + H^+, 255.0938. $C_{12}H_{17}NO_3S$ requires *M* + H^+, 255.0929).

1-Phenylsulfonyl-4-isopropylpyrrolidin-3-ol 9c. *Major diastereoisomer*; R_f 0.3 (Et_2O–light petroleum, 2:1); ν_{max}(thin film)/cm^{-1} 3515 (s), 2960 (m), 2875 (m), 1469 (m), 1447 (m), 1335 (s), 1164 (s), 1097 (m), 1075 (m), 1026 (m); δ_H(270 MHz, $CDCl_3$) 7.86–6.50 (5H, m, aromatics), 4.06 (1H, app. q, *J* 5.5, C*H*OH), 3.47–3.39 (2H, m, NCH_2), 3.13 (1H, dd, *J* 10.5 and 4.5, NC*H*), 2.93 (1H, dd, *J* 11 and 7.0, NC*H*), 2.05 (1H, br s, CHO*H*), 1.80–1.40 (2H, m, Me_2C*H* and Me_2CHC*H*), 0.92 (3H, d, *J* 7, *Me*CH), 0.83 (3H, d, *J* 7, *Me*CH); δ_C(67.5 MHz, $CDCl_3$) 135.9 (*C*=CH), 132.8, 129.0, 127.6 (*C*H=C), 73.4 (*C*HOH), 55.0, 49.9 (2 × NCH_2), 55.1 (Me_2CH*C*H), 29.3 (Me_2*C*H), 21.7, 21.3 (*Me*$_2$CH); *m*/*z* (CI, NH_3) 287 (M + NH_4^+, 22%), 270 (M + H^+, 100), 128 (26) (Found: M + H^+, 270.1150. $C_{13}H_{19}NO_3S$ requires *M* + H^+, 270.1164). *Minor diastereoisomer*; R_f 0.3 (Et_2O–light petroleum, 2:1); ν_{max}(thin film)/cm^{-1} 3516 (br, m), 2959 (m), 2874 (m), 1468 (m), 1146 (m), 1368 (s), 1333 (s), 1221 (m), 1163 (s), 1003 (s), 1054 (m), 757 (m); δ_H(270 MHz, $CDCl_3$) 7.89–7.45 (5H, m, aromatics), 4.24–4.22 (1H, m, C*H*OH), 3.53 (1H, app. t, *J* 8.5, NC*H*), 3.42–3.41 (2H, m, 2 × NC*H*), 3.04 (1H, app. t, *J* 10, NC*H*), 1.91 (1H, br s, CHO*H*), 1.77–1.47 (2H, m, Me_2C*H* and Me_2CHC*H*), 0.93 (3H, d, *J* 6.5, *Me*CH), 0.86 (3H, d, *J* 6.5, *Me*CH); δ_C(67.5 MHz, $CDCl_3$) 137.6 (*C*=CH), 133.1, 129.6, 128.0 (*C*H=C), 71.3 (*C*HOH), 57.6, 50.3 (2 × N*C*H_2), 52.5 (Me_2CH*C*H), 26.5 (Me_2*C*H), 21.9, 21.4 (*Me*$_2$CH); *m*/*z* (CI, NH_3) 287 (M + NH_4^+, 19%), 270 (M + H^+, 100), 219 (6), 128 (16) (Found: M + H^+, 270.1151. $C_{13}H_{19}NO_3S$ requires *M* + H^+, 270.1164).

1-Phenylsulfonyl-4-benzylpyrrolidin-3-ol 9d. *Major diastereoisomer* (Found: C, 64.14; H, 6.25; N, 4.39. $C_{17}H_{19}NO_3S$ requires C, 64.33; H, 6.03; N, 4.41%); R_f 0.3 (Et_2O–light petroleum, 2:1); ν_{max}(thin film)/cm^{-1} 3514 (br, s), 1446 (m), 1333 (m), 1161 (s), 1092 (m), 1056 (m); δ_H(270 MHz, $CDCl_3$) 7.78–7.04 (10H, m, aromatics), 4.03–4.02 (1H, m, C*H*OH), 3.42–3.28 (3H, m, 3 × NC*H*), 3.03 (1H, app. t, *J* 11, NC*H*), 2.72 (1H, dd, *J* 14 and 8, PhC*H*), 2.55 (1H, dd, *J* 14 and 7.5, PhC*H*), 2.23–2.15 (1H, m, PhCH_2C*H*), 1.57 (1H, br s, O*H*); δ_C(67.5 MHz, $CDCl_3$) 139.9, 137.5 (*C*=CH), 133.2, 133.1, 129.7, 129.5, 129.1, 128.9, 127.8, 127.7, 126.9, 128.8 (*C*H=C), 71.6 (*C*HOH), 57.2, 50.8 (2 × N*C*H_2), 46.5 (PhCH_2*C*H), 32.9 (Ph*C*H_2CH); *m*/*z* (CI, NH_3) 318 (M + H^+, 100%), 176 (48), 158 (18), 130 (14) (Found: M + H^+, 318.1166. $C_{17}H_{19}NO_3S$ requires *M* + H^+, 318.1164). *Minor diastereoisomer*; R_f 0.2 (Et_2O–light petroleum, 2:1); ν_{max}-(thin film)/cm^{-1} 3448 (br, s), 1446 (m), 1335 (s), 1160 (s), 1096 (m), 1074 (m), 1034 (m); δ_H(270 MHz, $CDCl_3$) 7.77–6.97 (10H, m, aromatics), 3.98–3.93 (1H, m, C*H*OH), 3.54 (1H, dd, *J* 11 and 5.5, NC*H*), 3.33 (1H, dd, *J* 10 and 7.0, NC*H*), 3.11 (1H, dd, *J* 11 and 3.5, NC*H*), 3.02 (1H, dd, *J* 10 and 5, NC*H*), 2.54 (1H, dd, *J* 14 and 7, PhC*H*), 2.36 (1H, dd, *J* 14 and 7, PhC*H*), 2.27–2.12 (1H, m, PhCH_2C*H*), 1.57 (1H, br s, O*H*); δ_C(67.5 MHz, $CDCl_3$) 138.6, 136.5 (*C*=CH), 132.8, 129.1, 128.7, 127.4, 126.6 (*C*H=C), 74.5 (*C*HOH), 54.3, 50.6 (2 × N*C*H_2), 48.0 (PhCH_2*C*H), 32.9 (Ph*C*H_2CH); *m*/*z* (CI, NH_3) 335 (M + NH_4^+, 14%), 318 (M + H^+, 100), 247 (8), 176 (32), 158 (18) (Found: M + H^+, 318.1166. $C_{17}H_{19}NO_3S$ requires *M* + H^+, 318.1164).

General procedure for oxidation and cyclisation of alcohols 7c–d

DMSO (1.74–5.44 mmol) was added dropwise to a solution of $(COCl)_2$ (0.88–2.73 mmol) in dry CH_2Cl_2 (10–20 cm^3) at −60 °C under nitrogen and the resulting mixture was stirred for 0.25 h at the same temperature. A solution of alcohol **7c**–**d** (0.29–1.36 mmol) in dry CH_2Cl_2 (5 cm^3) was added dropwise and the reaction was stirred for 0.5 h. Et_3N (2.03–6.80 mmol) was then added dropwise and the mixture was stirred for 0.5 h while warming to 0 °C. The suspension was poured into water (50 cm^3) and the mixture was extracted with Et_2O (2 × 20 cm^3). The organic extracts were washed with more water, dried ($MgSO_4$) and evaporated to give **10a**–**b** as a pale yellow liquid. This was immediately dissolved in degassed benzene (3–25 cm^3) and Bu_3SnH (0.58–1.86 mmol) and AIBN (0.03–0.30 mmol) were added in degassed benzene (0.5 cm^3) under a nitrogen atmosphere. The reaction mixture was then heated at reflux until starting material was consumed (2–12 h) [additional portions of AIBN (0.1 mmol) were added at 2 h intervals if required], then concentrated *in vacuo* and the crude product was separated by flash column chromatography (silica).

1-Phenylsulfonyl-3-benzylpiperidin-4-ol 11a. Following the general procedure, alcohol **7d** (96 mg, 0.29 mmol) was oxidised to aldehyde **10a**; ν_{max}(thin film)/cm^{-1} 2924 (s), 2554 (m), 1722 (s), 1448 (m), 1338 (m), 1559 (s); δ_H(270 MHz, $CDCl_3$) 9.74 (1H, d, *J* 1, C*H*O), 7.86–7.20 (5H, m, aromatics), 6.42 (1H, d, *J* 16, PhC*H*=CH), 5.96 (1H, dt, *J* 16 and 7, PhCH=C*H*), 3.97 (2H, d, *J* 7, NCH_2CH=CH), 3.48 (2H, t, *J* 7, NCH_2CH_2), 2.85 (2H, t, *J* 7, NCH_2CH_2). Crude **10a** was then treated with Bu_2SnH (167 mg, 0.58 mmol) and AIBN (5 mg, 0.03 mmol) and flash column chromatography (silica; Et_2O–light petroleum, 4:1) afforded piperidinol **11a** (55 mg, 56%) as separable diastereoisomers in the ratio 1.3:1 and alcohol **7d** (4 mg, 4%) which was inseparable from the major diastereoisomer. *Major diastereoisomer*; R_f 0.3 (Et_2O–light petroleum, 4:1); ν_{max}(thin film)/cm^{-1} 3454 (br, s), 1452 (w), 1334 (m), 1161 (s), 1085 (m), 1062 (m), 1019 (m), 751 (m); δ_H(270 MHz, $CDCl_3$) 7.69–7.09 (10H, m, aromatics), 3.64 (1H, m, C*H*OH), 3.41–3.27 (2H, m, 2 × NC*H*), 2.78–2.61 (1H, m, NC*H*), 2.56–2.48 (3H, m, PhCH_2 and NC*H*), 2.01–1.95 (1H, m, PhCH_2C*H*), 1.73–1.68 (2H, m, CH_2CH_2CH_2), 1.52 (1H, s, O*H*); δ_C(67.5 MHz, $CDCl_3$) 139.0, 136.2 (*C*=CH), 133.7, 129.0, 128.6, 128.4, 127.9, 127.5, 126.3 (*C*H=C), 64.7 (*C*HOH), 45.7 (N*C*H_2), 42.1 (PhCH_2*C*H), 41.1 (N*C*H_2), 34.8, 32.3 (Ph*C*H_2CH and CH_2*C*H_2CH_2); *m*/*z* (CI, NH_3) 349 (M + NH_4^+, 37%), 332 (M + H^+, 100), 192 (49), 172 (12) (Found: M + H^+, 332.1314. $C_{18}H_{21}NO_3S$ requires *M* + H^+, 332.1320). *Minor diastereoisomer*; R_f 0.2 (Et_2O–light petroleum, 4:1); ν_{max}(thin film)/cm^{-1} 3454 (br, s), 1542 (m), 1334 (m), 1161 (s), 1085 (m), 1062 (m), 1019 (m), 751 (m); δ_H(270 MHz, $CDCl_3$) 7.79–7.08 (10H, m, aromatics), 3.44–3.22 (2H, m, C*H*OH and NC*H*), 2.88 (1H, dd, *J* 14 and 5, NC*H*), 2.72–2.29 (3H, m, NC*H* and

PhCH_2), 1.98–1.77 (2H, m, NCH and PhCH$_2$CH), 1.69–1.51 (2H, m, CH$_2$CH_2CH$_2$), 1.49 (1H, br s, OH); δ_C(67.5 MHz, CDCl$_3$) 139.4, 136.7 (*C*=CH), 133.2, 129.0, 128.5, 127.5, 126.8 (*C*H=C), 70.6 (*C*HOH), 47.7, 44.2 (2 × N*C*H$_2$), 44.6 (PhCH$_2$*C*H), 36.4, 32.4 (Ph*C*H$_2$CH and CH$_2$*C*H$_2$CH$_2$); *m*/*z* (CI, NH$_3$) 349 (M + NH$_4^+$, 45%), 332 (M + H$^+$, 100), 233 (10), 192 (55), 172 (16) (Found: M + H$^+$, 332.1313. $C_{18}H_{21}NO_3S$ requires *M* + H$^+$, 332.1320).

Oxidation and radical cyclisation of 3-(*N*-allyl-*N*-phenylsulfonylamino)propanol 7c

Following the general procedure, alcohol **7c** (237 mg, 0.93 mmol) was oxidised to aldehyde **10b**; δ_H(270 MHz, CDCl$_3$) 9.69 (1H, t, *J* 1, C*H*O), 7.77–7.43 (5H, m, aromatics), 5.62–5.49 (2H, m, CH_2=CH), 5.12 (1H, app. t, *J* 8, CH$_2$=CH), 3.75 (2H, d, *J* 6.5, NCH_2CH=CH), 3.36 (2H, t, *J* 7.5, NCH_2CH$_2$), 2.76 (2H, td, *J* 7.5 and 1, NCH$_2$CH_2CHO). Crude **10b** was then treated with Bu$_3$SnH (541 mg, 1.86 mmol) and AIBN (15 mg, 0.10 mmol) and flash column chromatography of the residue (silica; Et$_2$O–light petroleum, 4:1), afforded piperidinol **11b** (98 mg, 40%) as separable diastereoisomers in the ratio 1.2:1, azepane **12** (18 mg, 8%) and alcohol **7c** (16 mg, 7%).

1-Phenylsulfonyl-3-methylpiperidin-4-ol 11b. *Major diastereoisomer* (Found: C, 56.31; H, 6.98; N, 5.39. $C_{12}H_{17}NO_3S$ requires C, 56.45; H, 6.71; N, 5.49%); R_f 0.3 (Et$_2$O–light petroleum, 4:1); ν_{max}(thin film)/cm^{-1} 3450 (br, s), 1454 (w), 1331 (m), 1162 (s), 1089 (m), 1020 (m), 986 (w), 750 (m), 580 (w); δ_H(270 MHz, CDCl$_3$) 7.85–7.49 (5H, m, aromatics), 3.84–3.77 (2H, m, C*H*OH and NCH), 3.45–3.32 (1H, m, NCH), 2.80–2.70 (1H, m, NCH), 2.47 (1H, t, *J* 11, NCH), 1.98–1.89 (1H, m, MeCH), 1.86–1.80 (2H, m, CH$_2$CH_2CH$_2$), 1.59 (1H, br s, OH), 1.00 (3H, d, *J* 6.5, *Me*CH); δ_C(67.5 MHz, CDCl$_3$) 139.5 (*C*=CH), 132.8, 128.9, 127.5 (*C*H=C), 67.2 (*C*HOH), 47.0 (N*C*H$_2$CH), 40.8 (N*C*H$_2$CH$_2$), 34.9 (Me*C*H), 32.9 (CH$_2$*C*H$_2$CH$_2$), 14.1 (*Me*CH); *m*/*z* (CI, NH$_3$) 273 (M + NH$_4^+$, 9%), 256 (M + H$^+$, 100), 116 (56) (Found: M + H$^+$, 256.1004. $C_{12}H_{17}NO_3S$ requires *M* + H$^+$, 256.1007). *Minor diastereoisomer*; R_f 0.24 (Et$_2$O–light petroleum; 4:1); ν_{max}(thin film)/cm^{-1} 3394 (br, s), 2942 (m), 1451 (w), 1337 (m), 1164 (s), 1089 (m), 1057 (m), 1021 (m), 753 (w); δ_H(270 MHz, CDCl$_3$) 7.78–7.51 (5H, m, aromatics), 3.72–3.58 (2H, m, C*H*OH, NCH), 3.15 (1H, dd, *J* 9.5 and 4, NCH), 2.49 (1H, td, *J* 11.5 and 3, NCH), 2.14 (1H, dd, *J* 11.5 and 10, NCH), 2.02–1.93 (1H, m, MeCH), 1.77–1.50 (3H, m, CH$_2$CH_2CH$_2$ and CHOH), 0.95 (3H, d, *J* 6.5, *Me*CH); δ_C(67.5 MHz, CDCl$_3$) 136.4 (*C*=CH), 132.8, 129.2, 127.7 (*C*H=C), 73.2 (*C*HOH), 50.7 (N*C*H$_2$CH), 44.8 (N*C*H$_2$CH$_2$), 38.2 (Me*C*H), 33.1 (CH$_2$*C*H$_2$CH$_2$), 15.1 (*Me*CH); *m*/*z* (CI, NH$_3$) 273 (M + NH$_4^+$, 22%), 256 (M + H$^+$, 100), 114 (26) (Found: M + H$^+$, 256.1003. $C_{12}H_{17}NO_3S$ requires *M* + H$^+$, 256.1007).

1-Phenylsulfonyl-4-hydroxyazepane 12. R_f 0.2 (Et$_2$O–light petroleum, 4:1); ν_{max}(thin film)/cm^{-1} 3439 (br, s), 1448 (w), 1329 (m), 1158 (s), 1092 (m), 1042 (w), 730 (w), 579 (w); δ_H(270 MHz, CDCl$_3$) 7.82–7.45 (5H, m, aromatics), 3.99–3.92 (1H, m, C*H*OH), 3.44–3.15 (4H, m, 2 × NCH_2), 2.07–1.60 (7H, m, NCH$_2$CH_2CH, CH$_2$CH$_2$CH_2CH, CH$_2$CH_2CH$_2$ and CHOH); δ_C(67.5 MHz, CDCl$_3$) 139.1 (*C*=CH), 132.4, 129.1, 127.0 (*C*H=C), 73.0 (*C*HOH), 48.8, 42.6 (2 × N*C*H$_2$), 37.9, 34.8 (2 × *C*H$_2$CHOH), 22.4 (CH$_2$*C*H$_2$CH$_2$); *m*/*z* (CI, NH$_3$) 273 (M + NH$_4^+$, 7%), 256 (M + H$^+$, 78), 238 (10), 114 (100), 96 (15), 85 (25) (Found: M + H$^+$, 256.1004. $C_{12}H_{17}NO_3S$ requires *M* + H$^+$, 256.1007).

Oxidation and cyclisation of 2-(*N*-phenylsulfonyl-*N*-prop-2-ynylamino)ethanol 13

Following the general procedure, alcohol **13** (326 mg, 1.36 mmol) was oxidised to the amino aldehyde; δ_H(270 MHz, CDCl$_3$) 9.68 (1H, s, C*H*O), 7.71–7.05 (5H, m, aromatics), 4.05 (2H, d, *J* 2.5, NCH_2C≡C), 3.97 (2H, s, NCH_2CHO), 2.02 (1H, t, *J* 2.5, C≡CH). The crude aldehyde was immediately treated with Bu$_3$SnH (594 mg, 2.04 mmol) and purification by flash column chromatography (silica; light petroleum–Et$_2$O, 1:1) afforded stananne **14** (102 mg, 14%) and alcohol **13** (104 mg, 32%). *Stannane* **14**. R_f 0.4 (light petroleum–Et$_2$O, 1:1); δ_H(270 MHz, CDCl$_3$) 7.86–7.52 (5H, m, aromatics), 6.01 (1H, d, *J* 2, C=C*H*Sn), 4.35–4.31 (1H, m, C*H*OH), 3.82 (1H, dd, *J* 14 and 2, NCH), 3.77 (1H, dd, *J* 14 and 6, NCH), 3.48 (1H, dd, *J* 10.5 and 5.5, NC*H*CH), 3.27 (1H, dd, *J* 10.5 and 5.5, NC*H*CH), 1.68–1.18 [18H, m, 3 × Sn(CH_2)$_3$Me], 0.87 [9H, t, *J* 7.5, 3 × Sn(CH$_2$)$_3$*Me*]; δ_C(67.5 MHz, CDCl$_3$) 154.0 (*C*=CHSn), 135.6 (*C*=CH), 132.9, 129.1, 127.8, 126.8 (*C*H=C, C=*C*HSn), 72.6 (*C*HOH), 56.1, 52.9 (2 × N*C*H$_2$), 28.9, 27.2 [SnCH$_2$(*C*H$_2$)$_2$Me], 13.6 [SnCH$_2$(CH$_2$)$_2$*Me*], 10.5 [Sn*C*H$_2$(CH$_2$)$_2$Me]; *m*/*z* (CI, NH$_3$) 529 (^{119}M + H$^+$, 68%), 472 (77), 433 (18), 388 (16), 358 (15), 330 (15), 308 (39), 291 (36), 257 (21), 240 (100) (Found: ^{116}M + H$^+$, 526.1748. $C_{23}H_{39}NO_3SSn$ requires ^{116}*M* + H$^+$, 526.1755).

General procedure for ozonolysis of 7a and 7c

To a solution of alkene **7a** or **7c** (3.41–43.6 mmol) in MeOH at −78 °C was passed ozone until the solution became pale blue. A stream of oxygen, followed by nitrogen was then passed through the solution for 0.2 h. The reaction mixture was then treated with DMS (6.82–87.2 mmol), warmed to room temperature and stirred under a nitrogen atmosphere for 0.5 h. The methanol was then removed *in vacuo* and the residue was purified by column chromatography (silica) to afford lactol **16**–**17** (81–90%).

2-Hydroxy-4-phenylsulfonylmorpholine 16. Mp 191–193 °C (Found: C, 49.51; H, 5.44; N, 5.42; S, 13.15. $C_{10}H_{13}NO_4S$ requires C, 49.37; H, 5.39; N, 5.76; S, 13.18%); R_f 0.4 (Et$_2$O–light petroleum, 9:1); ν_{max}(thin film)/cm^{-1} 3467–3444 (br, s), 1636 (w), 1449 (m), 1346 (s), 1271 (s), 1168 (s), 1122 (m), 1090 (s), 1056 (m), 967 (s); δ_H(270 MHz, CDCl$_3$) 7.83–7.53 (5H, m, aromatics), 4.96 (1H, dd, *J* 5.5 and 2.5, C*H*OH), 4.07–3.99 (1H, m, NCH), 3.72–3.64 (1H, m, NCH), 3.30 (1H, dd, *J* 11.5 and 1.5, NCH), 3.16–3.09 (1H, m, CH_2O), 2.90–2.82 (1H, m, CH_2O), 2.70 (1H, dd, *J* 11.5 and 5.5, NCH), 1.71 (1H, br s, CHOH); δ_C(67.5 MHz, CDCl$_3$) 135.1 (*C*=CH), 133.3, 129.3, 127.8 (*C*H=C), 91.1 (*C*HOH), 61.6 (*C*H$_2$O), 50.2, 45.0 (2 × N*C*H$_2$); *m*/*z* (CI, NH$_3$) 261 (M + NH$_4^+$, 58%), 244 (M + H$^+$, 73), 226 (75), 102 (100) (Found: M + H$^+$, 244.0640. $C_{10}H_{13}NO_4S$ requires *M* + H$^+$, 244.0644).

2-Hydroxy-1,4-oxazepane 17. R_f 0.2 (Et$_2$O–light petroleum, 4:1); ν_{max}(thin film)/cm^{-1} 3460–3358 (m), 1447 (m), 1333 (s), 1158 (s), 1092 (s), 1044 (s), 1027 (s); δ_H(270 MHz, CDCl$_3$) 7.82–7.50 (5H, m, aromatics), 5.21 (1H, dd, *J* 7.5 and 4, C*H*OH), 4.06–3.97 (1H, m, NCH), 3.87–3.61 (3H, m, 3 × NCH), 3.04–2.85 (3H, m, CH_2O and CHOH), 2.04–1.80 (2H, m, CH$_2$CH_2-CH$_2$); δ_C(67.5 MHz, CDCl$_3$) 139.0 (*C*=CH), 132.7, 129.1, 126.9 (*C*H=C), 94.3 (*C*HOH), 60.9 (*C*H$_2$O), 53.5, 49.0 (2 × N*C*H$_2$), 30.6 (CH$_2$*C*H$_2$CH$_2$); *m*/*z* (CI, NH$_3$) 275 (M + NH$_4^+$, 81%), 257 (M + H$^+$, 100), 240 (35), 233 (9), 219 (15) (Found: M + NH$_4^+$, 275.1067. $C_{11}H_{15}NO_4S$ requires *M* + NH$_4^+$, 275.1066).

General procedure for the preparation of alkenes 18a–d

To a solution of lactol **16**–**17** (1.15–2.91 mmol) in dry CH$_2$Cl$_2$ (10–25 cm^3) at room temperature was added Ph$_3$P=CHCO$_2$Et (2.30–5.82 mmol). The reaction was then heated at reflux under a nitrogen atmosphere until the starting material had been consumed as shown by TLC (8–12 h). The CH$_2$Cl$_2$ was removed *in vacuo* and Et$_2$O (25 cm^3) added. A white precipitate was formed which was removed by filtering the mixture through Celite. The filtrate was then concentrated and column chromatography (silica) afforded the desired alkenes **18a**–**d** (24–31%).

(*Z*)-Ethyl 4-[*N*-phenylsulfonyl-*N*-(2-hydroxyethyl)amino]but-2-enoate 18a. R_f 0.3 (Et$_2$O–light petroleum, 9:1); ν_{max}(thin film)/cm^{-1} 3518–3427 (m), 2392 (m), 1711 (s), 1411 (m), 1336 (s), 1164 (s), 1093 (m), 1031 (m); δ_H(270 MHz, CDCl$_3$) 7.87–7.51 (5H, m, aromatics), 6.25 (1H, dt, *J* 11.5 and 6, NCH$_2$CH=C), 5.86 (1H, d, *J* 11.5, CH$_2$OCOCH=C), 4.46 (2H, d, *J* 6, NCH_2-CH), 4.16 (2H, q, *J* 7, MeCH_2CO$_2$), 3.76 (2H, t, *J* 5.5, CH_2O),

3.32 (2H, t, *J* 5.5, NCH_2CH$_2$), 2.43 (1H, br s, CH$_2$O*H*), 1.27 (3H, t, *J* 7, *Me*CH$_2$CO); δ_C(67.5 MHz, CDCl$_3$) 165.9 (*C*O$_2$CH$_2$), 145.8 (NCH$_2$*C*H=C), 139.0 (*C*=CH), 132.9, 129.3, 127.2 (*C*H=C), 121.8 (CH$_2$CO$_2$*C*H=C), 61.0, 60.5 (*C*H$_2$CO$_2$CH=C and *C*H$_2$O), 51.3, 48.0 (2 × N*C*H$_2$), 14.2 (*Me*CH$_2$); *m*/*z* (CI, NH$_3$) 331 (M + NH$_4^+$, 18%), 314 (M + H$^+$, 100), 268 (11), 219 (12), 202 (9) (Found: M + H$^+$, 314.1055. $C_{14}H_{19}NO_5S$ requires *M* + H$^+$, 314.1062).

(*E*)-Ethyl 4-[*N*-phenylsulfonyl-*N*-(2-hydroxyethyl)amino]but-2-enoate 18b. R_f 0.2 (Et$_2$O–light petroleum, 9 : 1); ν_{max}(thin film)/cm^{-1} 3506–3455 (m), 2929 (m), 1715 (s), 1660 (m), 1446 (m), 1336 (s), 1272 (s), 1160 (s), 1089 (m), 1039 (m); δ_H(270 MHz, CDCl$_3$) 7.87–7.51 (5H, m, aromatics), 6.72 (1H, dt, *J* 16 and 6, NCH$_2$C*H*=C), 5.92 (1H, d, *J* 16, CH$_2$OCOC*H*=C), 4.17 (2H, q, *J* 7.5, MeC*H*$_2$CO$_2$), 4.06 (1H, d, *J* 6, NC*H*$_2$CH), 3.76 (2H, t, *J* 5.5, C*H*$_2$O), 3.30 (2H, t, *J* 5.5, NC*H*$_2$CH$_2$), 2.16 (1H, br s, CH$_2$O*H*), 1.27 (3H, t, *J* 7.5, *Me*CH$_2$CO); δ_C(67.5 MHz, CDCl$_3$) 165.6 (*C*O$_2$CH$_2$), 142.1 (NCH$_2$*C*H=C), 139.1 (*C*=CH), 133.2, 129.3, 127.2, (*C*H=C), 124.2 (CH$_2$OCO*C*H=C), 60.9, 60.6 (*C*H$_2$CO$_2$CH=C and *C*H$_2$O), 50.3, 50.0 (2 × N*C*H$_2$), 14.2 (*Me*CH$_2$); *m*/*z* (CI, NH$_3$) 331 (M + NH$_4^+$, 100%), 314 (M + H$^+$, 63), 282 (12), 268 (11), 219 (61), 202 (36), 172 (21) (Found: M + H$^+$, 314.1068. $C_{14}H_{19}NO_5S$ requires *M* + H$^+$, 314.1062).

(*Z*)-Ethyl 4-[*N*-phenylsulfonyl-*N*-(3-hydroxypropyl)amino]but-2-enoate 18c. R_f 0.4 (light petroleum–EtOAc, 3 : 2); ν_{max}(thin film)/cm^{-1} 3529–3439 (m), 2943 (m), 1715 (s), 1446 (m), 1331 (s), 1280 (m), 1163 (s), 1094 (m), 1042 (w); δ_H(270 MHz, CDCl$_3$) 7.86–7.50 (5H, m, aromatics), 6.19 (1H, dt, *J* 11.5 and 6, NCH$_2$C*H*=C), 5.84 (1H, d, *J* 11.5, CH$_2$CO$_2$C*H*=C), 4.44 (2H, d, *J* 6, NC*H*$_2$CH), 4.16 (2H, q, *J* 7, MeC*H*$_2$CO$_2$), 3.80 (2H, t, *J* 6, C*H*$_2$O), 3.30 (2H, t, *J* 6, NC*H*$_2$CH$_2$), 2.00 (1H, br s, CH$_2$O*H*), 1.75 (2H, quintet, *J* 6, CH$_2$C*H*$_2$CH$_2$), 1.28 (3H, t, *J* 7, *Me*CH$_2$); δ_C(67.5 MHz, CDCl$_3$) 165.9 (*C*O$_2$CH$_2$), 146.1 (NCH$_2$*C*H=C), 139.2 (*C*=CH), 132.8, 129.3, 127.1 (*C*H=C), 121.5 (CH$_2$OCO*C*H=C), 60.5, 58.7 (*C*H$_2$CO$_2$CH=C and *C*H$_2$O), 47.1, 45.7 (2 × N*C*H$_2$), 30.9 (CH$_2$*C*H$_2$CH$_2$), 14.2 (*Me*CH$_2$); *m*/*z* (CI, NH$_3$) 345 (M + NH$_4^+$, 15%), 328 (M + H$^+$, 61), 275 (65), 257 (100), 240 (44), 216 (11), 186 (14), 160 (12) (Found: M + NH$_4^+$, 328.1224. $C_{15}H_{21}NO_5S$ requires *M* + NH$_4^+$, 328.1219).

(*E*)-Ethyl 4-[*N*-phenylsulfonyl-*N*-(3-hydroxypropyl)amino]but-2-enoate 18d. R_f 0.3 (light petroleum–EtOAc, 3 : 2); ν_{max}(thin film)/cm^{-1} 3531–3442 (m), 2941 (w), 1716 (s), 1446 (w), 1335 (m), 1276 (m), 1161 (s), 1115 (w), 1091 (m), 1042 (m); δ_H(270 MHz, CDCl$_3$) 7.94–7.59 (5H, m, aromatics), 6.80 (1H, dt, *J* 15.5 and 6, NCH$_2$C*H*=C), 5.98 (1H, d, *J* 15.5, CH$_2$CO$_2$C*H*=C), 4.25 (2H, q, *J* 7.5, MeC*H*$_2$), 4.06 (2H, d, *J* 6, NC*H*$_2$CH), 3.81 (2H, t, *J* 6, C*H*$_2$O), 3.39 (2H, t, *J* 5.5, NC*H*$_2$CH$_2$), 2.11 (1H, br s, CH$_2$O*H*), 1.82 (2H, quintet, *J* 6, CH$_2$C*H*$_2$CH$_2$), 1.35 (3H, t, *J* 7.5, *Me*CH$_2$); δ_C(67.5 MHz, CDCl$_3$) 165.9 (*C*O$_2$CH$_2$), 142.5 (NCH$_2$*C*H=C), 139.7 (*C*=CH), 133.7, 129.3, 127.4 (*C*H=C), 124.7 (CH$_2$OCO*C*H=C), 61.1, 59.2 (*C*H$_2$OCOCH=C and *C*H$_2$O), 49.4, 45.3 (2 × N*C*H$_2$), 31.2 (CH$_2$*C*H$_2$CH$_2$), 14.6 (*Me*CH$_2$); *m*/*z* (CI, NH$_3$) 345 (M + NH$_4^+$, 100%), 328 (M + H$^+$, 57), 275 (12), 233 (62), 216 (34) (Found: M + H$^+$, 328.1223. $C_{15}H_{21}NO_5S$ requires *M* + H$^+$, 328.1219).

Oxidation and cyclisation of (*Z*)-ethyl 4-[*N*-phenylsulfonyl-*N*-(2-hydroxyethyl)amino]but-2-enoate 18a

Following the general procedure, alcohol **18a** (169 mg, 0.54 mmol) was oxidised and passed through a silica plug (Et$_2$O) to afford (*Z*)-*ethyl* 4-(N-*formylmethyl*-N-*phenylsulfonylamino*)*but*-2-*enoate* **19a** (109 mg, 65%); δ_H(270 MHz, CDCl$_3$) 9.58 (1H, t, *J* 1, C*H*O), 7.77–7.42 (5H, m, aromatics), 6.23 (1H, dt, *J* 11 and 6, NCH$_2$C*H*=CH), 5.89 (1H, d, *J* 16, OCOC*H*=CH), 4.38 (2H, d, *J* 6, NC*H*$_2$CH), 4.15 (2H, q, *J* 7, OC*H*$_2$Me), 3.91 (2H, d, *J* 1, NC*H*$_2$CHO), 1.28 (3H, t, *J* 7, *Me*CH$_2$CO); *m*/*z* (CI, NH$_3$) 329 (M + NH$_4^+$, 10%), 312 (M + H$^+$, 14) (Found: M + NH$_4^+$, 329.1176. $C_{14}H_{17}NO_5S$ requires *M* + NH$_4^+$, 329.1171). Aldehyde **19a** was then reacted with Bu$_3$SnH (236 mg, 0.81 mmol) and AIBN (9 mg, 0.05 mmol) and after 2 h the solvent was removed *in vacuo* and flash column chromatography (silica; Et$_2$O) yielded **20a** (30 mg, 27%) and **21a** (27 mg, 29%).

(3*R,4*S**)-1-Phenylsulfonyl-4-(ethoxycarbonylmethyl)pyrrolidin-3-ol 20a.** R_f 0.3 (Et$_2$O); ν_{max}(thin film)/cm^{-1} 3446 (br, m), 1726 (s), 1340 (s), 1268 (m), 1163 (s), 1097 (m), 1030 (m), 606 (m), 574 (m); δ_H(270 MHz, CDCl$_3$) 7.84–7.52 (5H, m, aromatics), 4.13 (2H, q, *J* 7, OC*H*$_2$Me), 4.03–3.97 (1H, m, C*H*OH), 3.64 (1H, dd, *J* 10.5 and 6.5, NC*H*), 3.58–3.49 (1H, m, NC*H*), 3.09 (1H, dd, *J* 10.5 and 5.5, NC*H*), 3.04–2.95 (2H, m, NC*H* and C*H*CH$_2$CO), 2.34 (2H, d, *J* 5, CHC*H*$_2$CO), 1.25 (3H, t, *J* 7, *Me*CH$_2$CO); δ_C(67.5 MHz, CDCl$_3$) 172.6 (*C*O$_2$CH$_2$), 136.1 (*C*=CH), 132.9, 129.1, 127.6 (*C*H=C), 74.9 (*C*HOH), 61.2 (O*C*H$_2$Me), 54.1, 51.2 (2 × N*C*H$_2$), 42.4 (*C*HCH$_2$CO), 36.0 (CH*C*H$_2$CO), 14.1 (*Me*CH$_2$CO); *m*/*z* (CI, NH$_3$) 331 (M + NH$_4^+$, 36%), 314 (M + H$^+$, 100), 174 (36) (Found: M + H$^+$, 314.1064. $C_{14}H_{19}NO_5S$ requires *M* + H$^+$, 314.1062).

(1*R,5*R**)-7-Phenylsulfonyl-2-oxa-7-azabicyclo[3.3.0]octan-3-one 21a.** R_f 0.1 (Et$_2$O); ν_{max}(thin film)/cm^{-1} 1779 (s), 1447 (w), 1345 (m), 1166 (s), 1105 (m), 1043 (m), 1023 (m); δ_H(270 MHz, CDCl$_3$) 7.77–7.47 (5H, m, aromatics), 4.90 (1H, t, *J* 7, CH$_2$-C*H*OCO), 3.55 (1H, d, *J* 11.5, NC*H*), 3.20–3.08 (3H, m, 3 × NC*H*), 3.06–2.95 (1H, m, CH$_2$C*H*CH$_2$), 2.75 (1H, dd, *J* 18.5 and 9.5, CHC*H*CO$_2$), 2.39 (1H, dd, *J* 18.5 and 3.5, CHC*H*CO$_2$); δ_C(67.5 MHz, CDCl$_3$) 175.4 (*C*O$_2$CH$_2$), 134.8 (*C*=CH), 133.5, 129.4, 127.9 (*C*H=C), 81.8 (CH$_2$*C*HCO), 54.0, 53.7 (2 × N*C*H$_2$), 37.6 (CH$_2$*C*HCH$_2$), 34.0 (CH*C*H$_2$CO); *m*/*z* (CI, NH$_3$) 285 (M + NH$_4^+$, 100%), 160 (11), 145 (9), 128 (77) (Found: M + NH$_4^+$, 285.0913. $C_{12}H_{13}NO_4S$ requires *M* + NH$_4^+$, 285.0990).

Oxidation and cyclisation of (*Z*)-ethyl 4-[*N*-phenylsulfonyl-*N*-(3-hydroxypropyl)amino]but-2-enoate 18c

Following the general procedure, alcohol **18c** (153 mg, 0.47 mmol) was oxidised to afford crude aldehyde **19c** which was immediately reacted with Bu$_3$SnH (205 mg, 0.91 mmol) and AIBN (16 mg, 0.1 mmol). After 3 h, the solvent was removed *in vacuo* to give crude product which was purified by flash column chromatography (silica; Et$_2$O) to afford **20b** (36 mg, 23%) and **21b** (34 mg, 25%) as colourless oils.

(4*R,5*R**)-1-Phenylsulfonyl-5-(ethoxycarbonylmethyl)piperidin-4-ol, 20b.** R_f 0.3 (Et$_2$O); ν_{max}(thin film)/cm^{-1} 3515 (s), 1727 (s), 1496 (m), 1467 (m), 1335 (s), 1310 (s), 1291 (m), 1270 (m), 1166 (s), 1091 (m), 1025 (m), 970 (w); δ_H(270 MHz, CDCl$_3$) 7.93–7.59 (5H, m, aromatics), 4.24 (2H, q, *J* 5, OC*H*$_2$Me), 3.74–3.38 (3H, m, 2 × NC*H* and C*H*OH), 2.75–2.35 (4H, m, 2 × NC*H* and CHC*H*$_2$CO), 2.26–2.18 (1H, m, C*H*CH$_2$CO), 2.09–1.71 (3H, m, NCH$_2$C*H*$_2$ and CHO*H*), 1.23 (3H, t, *J* 5, *Me*CH$_2$CO); δ_C(67.5 MHz, CDCl$_3$) 172.7 (*C*O$_2$CH$_2$), 136.4 (*C*=CH), 132.9, 129.2, 127.5 (*C*H=C), 71.0 (*C*HOH), 60.9 (O*C*H$_2$Me), 48.4, 44.2 (2 × N*C*H$_2$), 39.7 (*C*HCH$_2$CO), 36.4, 32.7 (CH*C*H$_2$CO and CH$_2$*C*H$_2$CH$_2$), 14.2 (*Me*CH$_2$CO); *m*/*z* (CI, NH$_3$) 345 (M + NH$_4^+$, 4%), 328 (M + H$^+$, 100), 310 (22), 282 (11), 264 (6), 186 (28), 168 (65) (Found: M + H$^+$, 328.1226. $C_{15}H_{21}NO_5S$ requires *M* + H$^+$, 328.1219).

(1*R,5*S**)-7-Phenylsulfonyl-2-oxa-7-azabicyclo[4.3.0]nonan-3-one 21b.** R_f 0.3 (Et$_2$O); ν_{max}(thin film)/cm^{-1} 1781 (s), 1446 (s), 1345 (s), 1237 (m), 1166 (s), 930 (m); δ_H(270 MHz, CDCl$_3$) 7.84–7.53 (5H, m, aromatics), 4.56 (1H, dd, *J* 8 and 4, CH$_2$C*H*OCO), 3.69–3.52 (2H, m, 2 × NC*H*), 2.80–2.54 (3H, m, 2 × NC*H*, 1 × CHC*H*$_2$O), 2.29–2.01 (4H, m, 1 × CHC*H*$_2$O, CH$_2$C*H*$_2$CH$_2$ and CH$_2$C*H*CH$_2$); δ_C(67.5 MHz, CDCl$_3$) 175.6 (*C*O$_2$CH$_2$), 135.8 (*C*=CH), 133.2, 129.4, 127.6 (*C*H=C), 75.6 (CH$_2$*C*HOCO), 45.8, 41.1 (2 × N*C*H$_2$), 34.5 (CH$_2$*C*HCH$_2$), 34.4 (CH*C*H$_2$CO), 27.0 (CH$_2$*C*H$_2$CH$_2$); *m*/*z* (CI, NH$_3$) 299 (M + NH$_4^+$, 25%), 282 (M + H$^+$, 48), 264 (15), 268 (13), 267 (51), 149 (41), 140 (100) (Found: M + H$^+$, 282.0797. $C_{13}H_{15}NO_4S$ requires *M* + H$^+$, 282.0800).

2-{*N*-Phenylsulfonyl-*N*-[2-(2-oxotetrahydrofuran-3-ylidene)-ethyl]amino}ethanol 23

To a solution of the lactol **16** (1.50 g, 6.17 mmol) in dry CH_2Cl_2 (10 cm^3) at room temperature was added 3-triphenylphosphoranylidene-2-oxotetrahydrofuran **22** (2.35 g, 5.82 mmol). The reaction was then heated at reflux under a nitrogen atmosphere for 2 h, the CH_2Cl_2 was removed *in vacuo*, Et_2O (25 cm^3) was added and a white precipitate was observed to form. The mixture was then filtered through Celite, and the filtrate concentrated to afford a yellow oil. This oil was dissolved in dry CH_2Cl_2 (5 cm^3) and treated with Et_3N (0.69 g, 6.79 mmol), TBDMSCl (1.86 g, 12.34 mmol) and a catalytic quantity of DMAP. The mixture was then allowed to stir at room temperature for 4 h. Work-up and column chromatography (silica; Et_2O–light petroleum, 4:1) afforded the *O*-silyl ether (1.61 g, 61%) as a colourless oil. A solution of silyl ether (1.54 g, 3.63 mmol) in MeOH (20 cm^3), containing a catalytic quantity of *p*-TsOH was allowed to stir for 3 h at room temperature. Evaporation of the solvent *in vacuo* followed by column chromatography of the residue (silica; EtOAc) afforded the desired alcohol **23** (941 mg, 83%) as a colourless oil; R_f 0.3 (EtOAc); ν_{max}(thin film)/cm^{-1} 3452 (br, s), 2924 (w), 1751 (s), 1446 (w), 1332 (s), 1213 (s), 1159 (s), 1089 (w), 1031 (m); δ_H(270 MHz, $CDCl_3$) 7.86–7.50 (5H, m, aromatics), 6.56–6.49 (1H, m, CH_2CH=C), 4.40 (2H, t, *J* 7.5, CCH_2CH_2O), 4.13 (2H, d, *J* 7, NCH_2CH), 3.81 (2H, t, *J* 6, NCH_2CH_2O), 3.32 (2H, t, *J* 6, NCH_2CH_2), 2.98–2.91 (2H, m, CCH_2CH_2O); δ_C(67.5 MHz, $CDCl_3$) 170.7 (CO_2CH_2), 138.9 (*C*=CH), 134.0, 133.0, 129.2, 126.8 (*C*H=C, CH_2CH=C), 128.2 (*C*=$CHCH_2$), 65.7, 61.0 (2 × CH_2O), 50.4, 48.0 (2 × NCH_2), 24.8 (CCH_2CH_2O); *m*/*z* (CI, NH_3) 329 (M + NH_4^+, 100%), 312 (M + H^+, 32), 219 (19), 170 (16) (Found: M + NH_4^+, 329.1172. $C_{14}H_{17}NO_5S$ requires *M* + NH_4^+, 329.1171).

Oxidation and cyclisation of alcohol 23

Following the general procedure, alcohol **23** (233 mg, 0.72 mmol) was oxidised and immediately treated with Bu_3SnH (419 mg, 1.44 mmol) followed by flash column chromatography (silica; Et_2O) to afford three fractions containing **24** (69 mg, 31%) (shown to be a 1.3:1 mixture of inseparable diastereoisomers) as a pale yellow oil, **24** (38 mg, 17%) (single diastereoisomer) as a clear oil and **25** (12 mg, 6%) as a white solid.

1-Phenylsulfonyl-4-(2-oxotetrahydrofuran-3-yl)pyrrolidin-3-ol 24. *Major diastereoisomer* 1; R_f 0.2 (EtOAc–light petroleum, 4:1); ν_{max}(thin film)/cm^{-1} 3436 (br, s), 1760 (s), 1340 (m), 1162 (w); δ_H(270 MHz, $CDCl_3$) 7.85–7.15 (5H, m, aromatics), 4.15 (2H, t, *J* 8, CH_2OCO), 4.11–4.02 (3H, m, CHOH and 2 × NCH), 3.62 (1H, dd, *J* 10.5 and 5, NC*H*), 3.12 (1H, m, NC*H*), 2.72–2.68 (2H, m, CH_2CH_2OCO), 2.45–1.99 (2H, m, CH_2CHCH, CH_2CHCH), 1.78 (1H, br s, CHO*H*); δ_C(67.5 MHz, $CDCl_3$) 178.9 (CO_2CH_2), 137.0 (*C*=CH), 134.3, 130.6, 128.8 (*C*H=C), 72.4 (*C*HOH), 68.0 (CH_2CH_2OCO), 55.3, 50.7 (2 × NCH_2), 47.6, 41.6 (CH_2CHCH and CH_2CHCH), 28.4 (OCH_2CH_2CH); *m*/*z* (CI, NH_3) 329 (M + NH_4^+, 92%), 312 (M + H^+, 100), 172 (38), 170 (45) (Found: M + H^+, 312.0899. $C_{14}H_{17}NO_5S$ requires *M* + H^+, 312.0906). *Minor diastereoisomer* 2; the presence of this was indicated by ^1H NMR spectroscopy; δ_H(270 MHz, $CDCl_3$) 3.91 (1H, dd, *J* 11 and 5, NC*H*), 3.82 (1H, app. t, *J* 9, NC*H*); δ_C(67.5 MHz, $CDCl_3$) 180.0 (CO_2CH_2), 137.8 (*C*=CH), 134.2, 130.4, 128.6 (*C*H=C), 74.5 (*C*HOH), 68.2 (CH_2CH_2OCO), 57.5, 50.4 (2 × NCH_2), 46.1, 40.0 (CH_2CHCH, CH_2CHCH), 29.2 (OCH_2CH_2CH). *Diastereoisomer* 3; R_f 0.3 (EtOAc–light petroleum, 4:1); ν_{max}(thin film)/cm^{-1} 3489 (br, m), 1759 (s), 1336 (m), 1162 (w), 1021 (w); δ_H(270 MHz, $CDCl_3$) 7.91–7.10 (5H, m, aromatics), 4.42–4.14 (3H, m, CH_2OCO and CHOH), 3.78–3.61 (1H, m, NC*H*), 3.46 (1H, dd, *J* 10 and 8, NC*H*), 3.01 (1H, dd, *J* 10 and 7, NC*H*), 2.94 (1H, dd, *J* 10 and 8.5, NC*H*), 2.55–2.23 (2H, m, CH_2CH_2OCO), 2.10–1.86 (2H, m, CH_2CHCH and CH_2CHCH), 1.65 (1H, br s, CHO*H*); δ_C(67.5 MHz, $CDCl_3$) 179.3 (CO_2CH_2), 136.0 (*C*=CH), 133.1, 129.2, 127.5 (*C*H=C), 73.7 (*C*HOH), 67.7 (CH_2CH_2OCO), 53.7, 50.6 (2 × NCH_2), 46.7, 42.4 (CH_2CHCH and CH_2CHCH), 28.2 (OCH_2CH_2CH); *m*/*z* (CI, NH_3) 329 (M + NH_4^+, 100%), 312 (M + H^+, 71), 172 (26), 170 (34) (Found: M + H^+, 312.0902. $C_{14}H_{17}NO_5S$ requires *M* + H^+, 312.0906).

1-Phenylsulfonylamino-2-(2-oxotetrahyrofuran-3-ylidene)-ethane 25. R_f 0.8 (EtOAc–light petroleum, 4:1); ν_{max}(thin film)/cm^{-1} 3272 (s), 1751 (s), 1445 (m), 1327 (m), 1207 (m), 1160 (s), 1092 (w); δ_H(270 MHz, $CDCl_3$) 7.93–7.41 (5H, m, aromatics), 6.45–6.38 (1H, m, CH_2CHC=C), 4.81 (1H, t, *J* 6, N*H*), 4.29 (2H, t, *J* 7, CCH_2CH_2O), 3.76–3.70 (2H, m, NCH_2), 2.86–2.78 (2H, m, CH_2CH_2OCO); δ_C(67.5 MHz, $CDCl_3$) 170.3 (CO_2CH_2), 139.7 (*C*=CH), 133.3, 133.1, 129.3, 127.0 (*C*H=C and CH_2CH=C), 128.5 (CH=*C*CH_2), 73.7 (*C*HOH), 65.5 (CH_2CH_2OCO), 42.1 (NCH_2), 25.1 (OCH_2CH_2C); *m*/*z* (CI, NH_3) 285 (M + NH_4^+, 100%), 175 (73), 130 (36) (Found: M + NH_4^+, 285.0910. $C_{14}H_{13}NO_4S$ requires *M* + NH_4^+, 285.0909).

1,3-Dibenzyl-4-hydroxypyrrolidin-2-one 27

Following the general procedure, alcohol **26** (120 mg, 0.43 mmol) was oxidised to the aldehyde and immediately treated with Bu_3SnH (188 mg, 0.65 mmol). Column chromatography (silica; Et_2O) afforded **27** (43 mg, 37%) as a 2.1:1 mixture of diastereoisomers. *Major diastereoisomer*; R_f 0.4 (Et_2O); ν_{max}(thin film)/cm^{-1} 3376 (br, s), 1665 (s), 1604 (w), 1494 (m), 1451 (m), 1269 (m); δ_H(270 MHz, $CDCl_3$) 7.40–7.15 (10H, m, aromatics), 4.43 (2H, br s, $PhCH_2N$), 4.21–4.17 (1H, m, CHOH), 3.42–3.14 (2H, m, 2 × NC*H*), 3.05–2.72 (3H, m, $PhCH_2CH$ and $PhCH_2CH$), 2.17 (1H, br s, CHO*H*); δ_C(67.5 MHz, $CDCl_3$) 173.6 (NCO), 138.3, 135.9 (*C*=CH), 129.1, 128.8, 128.7, 128.0, 127.6, 126.7 (*C*H=C), 69.4 (*C*HOH), 52.8 (NCH_2), 46.4 ($PhCH_2$), 34.9 ($PhCH_2CH$); *m*/*z* (CI, NH_3) 282 (M + H^+, 100%), 192 (6), 91 (5) (Found: M + H^+, 282.1491. $C_{18}H_{19}NO_2$ requires *M* + H^+, 282.1491). *Minor diastereoisomer*—the presence of this was indicated by ^1H NMR spectroscopy; δ_H(270 MHz, $CDCl_3$) 4.41–4.12 (1H, m, CHOH), 2.76–2.67 (1H, m, $PhCH_2CH$); δ_C(67.5 MHz, $CDCl_3$) 172.1 (NCO), 138.9, 134.7 (*C*=CH), 72.1 (*C*HOH), 52.9 (NCH_2), 48.5 ($PhCH_2$), 32.2 ($PhCH_2CH$).

General procedure for the preparation of dienes 28a–b

Alcohol **8d** and **10a** (0.63–3.29 mmol) was oxidised under Swern conditions and then immediately reacted with (triphenylphosphoranylidene)propan-2-one (3.15–16.45 mmol) in dry CH_2Cl_2 (10–30 cm^3) under nitrogen at room temperature. After stirring overnight the solvent was removed *in vacuo* and the residue was dissolved in Et_2O (20–60 cm^3), filtered through Celite, washed with water and brine, dried ($MgSO_4$) and evaporated to afford crude product. Column chromatography (silica) afforded **28a–b** (64–72%) as a colourless oil.

(*E*)-5-(*N*-Phenylsulfonyl-*N*-cinnamylamino)pent-3-en-2-one 28a. R_f 0.5 (Et_2O–light petroleum, 3:2); ν_{max}(thin film)/cm^{-1} 3055 (w), 3028 (w), 2924 (w), 1665 (s), 1455 (m), 1337 (s), 1160 (s); δ_H(270 MHz, $CDCl_3$) 7.80–7.13 (10H, m, aromatics), 6.50 (1H, dt, *J* 16 and 6, CH=CHCOMe), 6.33 (1H, d, *J* 16, PhCH=CH), 6.04 (1H, d, *J* 16, CH=CHCOMe), 5.84 (1H, dt, *J* 16 and 7, PhCH=CH), 3.93–3.86 (4H, m, 2 × NCH_2), 2.10 (3H, s, CO*Me*); δ_C(67.5 MHz, $CDCl_3$) 197.7 (COMe), 141.3 (CH=CHCOMe), 139.8, 135.7 (*C*=CH), 132.9, 132.6 (PhCH=CH and CH=CHCOMe), 134.8, 129.3, 128.6, 128.2, 127.8, 127.1, 126.4 (*C*H=C), 122.9 (PhCH=CH), 50.2, 47.8 (2 × NCH_2), 27.1 (CO*Me*); *m*/*z* (CI, NH_3) 373 (M + NH_4^+, 6%), 356 (M + H^+, 19), 272 (20), 214 (33), 117 (100) (Found: M + H^+, 356.1309. $C_{20}H_{21}NO_3S$ requires *M* + H^+, 356.1320).

(*E*)-6-(*N*-Phenylsulfonyl-*N*-cinnamylamino)hex-3-en-2-one 28b. R_f 0.5 (Et_2O–light petroleum, 4:1); ν_{max}(thin film)/cm^{-1} 3060 (m), 3027 (m), 3004 (w), 2926 (m), 1674 (s), 1628 (m), 1146 (m), 1339 (m), 1257 (m), 1160 (s), 1091 (m), 974 (m), 736 (m); δ_H(270 MHz, $CDCl_3$) 7.96–7.34 (10H, m, aromatics), 6.81 (1H,

dt, *J* 16 and 7, C*H*=CHCOMe), 6.56 (1H, d, *J* 16, PhC*H*=CH), 6.14 (1H, d, *J* 16, CH=C*H*COMe), 6.05 (1H, dt, *J* 16 and 7, PhCH=C*H*), 4.08 (2H, t, *J* 7, NCH_2), 3.42 (2H, t, *J* 7, NCH_2), 3.57 (2H, app. q, *J* 7, CH_2CH_2CH), 2.30 (3H, s, CO*Me*); δ_C(67.5 MHz, $CDCl_3$) 198.2 (*C*OMe), 143.6 (*C*H=CHCOMe), 139.7, 135.8 (*C*=CH), 132.9, 132.7 (Ph*C*H=CH and CH=*C*HCOMe), 134.9, 129.5, 128.7, 128.1, 127.6, 127.0, 126.9 (*C*H=C), 123.9 (PhCH=*C*H), 50.2, 46.0 (2 × NCH_2), 31.9 (CH_2CH_2CH), 26.9 (CO*Me*); *m*/*z* (CI, NH_3) 387 ($M + NH_4^+$, 100%), 370 ($M + H^+$, 79), 271 (52), 228 (48), 117 (60) (Found: $M + H^+$, 370.1480. $C_{21}H_{23}NO_3S$ requires $M + H^+$, 370.1477).

General procedure for the cyclisation of dienes 28a–b

To a solution of diene **28a**–**b** (0.45–0.64 mmol) in degassed benzene (4.5–6.4 cm^3) under a nitrogen atmosphere was added Bu_3SnH (0.9–1.28 mmol) and AIBN (0.5–0.1 mmol) in degassed benzene (0.5 cm^3). The mixture was heated to 80 °C until the reaction was shown to be complete by TLC (2–4 h). The solvent was then removed *in vacuo* to give a yellow oil which was purified by flash column chromatography (silica) to afford **29a**–**b** (61–76%) as an inseparable mixture of diastereoisomers.

1-Phenylsulfonyl-3-(2-oxopropyl)-4-benzylpyrrolidine 29a. *Major diastereoisomer*; R_f 0.2 (Et_2O–light petroleum, 3 : 1); ν_{max}(thin film)/cm^{-1} 1713 (s), 1447 (w), 1340 (s), 1163 (s), 965 (w), 752 (w), 717 (w); δ_H(270 MHz, $CDCl_3$) 7.76–7.10 (10H, m, aromatics), 3.51 (1H, dd, *J* 10 and 7.5, NC*H*), 3.42–3.36 (1H, m, NC*H*), 3.28 (1H, dd, *J* 10 and 7, NC*H*), 3.13–2.80 (1H, m, C*H*CH_2CO), 2.77 (1H, dd, *J* 10 and 7.5, NC*H*), 2.61–2.05 (5H, m, PhCH_2CH, PhCH_2C*H* and CH_2CO), 2.07 (3H, s, CO*Me*); δ_C(67.5 MHz, $CDCl_3$) 208.0 (*C*OMe), 140.1, 136.6 (*C*H=C), 132.6, 128.9, 128.7, 128.4, 127.6, 127.4, 127.1 (*C*H=C), 54.1, 53.9 (2 × NCH_2), 51.1 (*C*H_2COMe), 39.9 (Ph*C*H_2), 37.0, 36.9 (PhCH_2*C*H and *C*HCH_2CO); *m*/*z* (CI, NH_3) 358 ($M + H^+$, 95%), 218 (100), 160 (11), 126 (6), 94 (7), 68 (23) (Found: $M + H^+$, 358.1486. $C_{20}H_{23}NO_3S$ requires $M + H^+$, 358.1477). *Minor diastereoisomer*—this was indicated by ^{1}H NMR spectroscopy; δ_H(270 MHz, $CDCl_3$) 3.39 (1H, dd, *J* 14 and 7, NC*H*), 2.82 (1H, dd, *J* 10 and 6.5, NC*H*), 2.10 (3H, s, CO*Me*); δ_C(67.5 MHz, $CDCl_3$) 207.8 (*C*OMe), 139.9, 136.1 (*C*H=C), 55.3, 54.0 (2 × NCH_2), 49.9 (*C*H_2COMe), 38.7 (Ph*C*H_2), 35.9, 34.7 (PhCH_2*C*H and *C*HCH_2CO).

1-Phenylsulfonyl-4-(2-oxopropyl)-5-benzylpiperidine 29b. *Major diastereoisomer*; R_f 0.3 (light petroleum–Et_2O, 3 : 1); ν_{max}(thin film)/cm^{-1} 1721 (s), 1448 (m), 1333 (m), 1215 (m), 1160 (s), 722 (m); δ_H(270 MHz, $CDCl_3$) 7.72–7.06 (10H, m, aromatics), 3.57–3.39 (2H, m, 2 × NC*H*), 2.86–2.00 (6H, m, 2 × NC*H*, CH_2COMe, PhCH_2C*H* and CH_2C*H*CH_2), 2.08 (3H, s, CO*Me*), 1.96–1.51 (3H, m, NCH_2CH_2 and CH_2C*H*CH_2); δ_C(67.5 MHz, $CDCl_3$) 207.4 (*C*OMe), 140.1, 136.6 (CH=*C*), 132.6, 128.9, 128.7, 128.5, 128.4, 127.5, 127.4, 126.4, 126.1 (*C*H=C), 49.7 (*C*H_2COMe), 46.9, 45.3 (2 × NCH_2), 41.0, 34.8 (PhCH_2*C*H and *C*HCH_2CO), 37.5 (Ph*C*H_2), 30.5 (CO*Me*), 30.3 ($CH_2CH_2CH_2$); *m*/*z* (CI, NH_3) 389 ($M + NH_4^+$, 14%), 372 ($M + H^+$, 100), 230 (26), 172 (6) (Found: $M + H^+$, 372.1632. $C_{21}H_{25}NO_3S$ requires $M + H^+$, 372.1633). *Minor diastereoisomer*—this was indicated by ^{1}H NMR spectroscopy; δ_H(270 MHz, $CDCl_3$) 3.74–3.69 (1H, m, NC*H*), 2.11 (3H, s, CO*Me*); δ_C(67.5 MHz, $CDCl_3$) 207.1 (*C*OMe), 138.8, 136.0 (*C*H=C), 48.7 (*C*H_2COMe), 46.3, 46.1 (2 × NCH_2), 39.7, 33.7 (PhCH_2*C*H and *C*HCH_2CO), 31.5 (Ph*C*H_2), 30.5 (CO*Me*), 26.7 ($CH_2CH_2CH_2$).

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