A stereochemically flexible approach to pyrrolidines based on 5-*endo-trig* iodocyclisations of homoallylic sulfonamides

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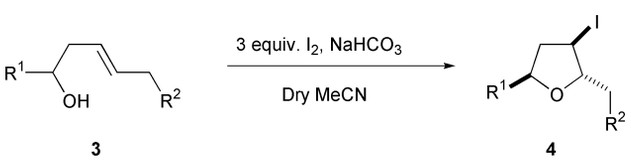
5-*endo-trig* Iodocyclisations of the (*E*)-homoallylic sulfonamides **24** in the presence of potassium carbonate give excellent yields of *trans*-2,5-disubstituted-3-iodopyrrolidines **36**. In the absence of base, these initial kinetic products undergo rapid isomerization to the corresponding *cis*-2,5-disubstituted pyrrolidines **37** by a ring opening–reclosure mechanism to these thermodynamic isomers. Octahydroindole derivatives **40** and **41** can be similarly obtained from the alk-2-enylcyclohexylsulfonamides **31** and **32**. Attempted 5-*endo-trig* cyclisations of homoallylic carbamates were generally unsuccessful and resulted instead in relatively inefficient 6-*exo* cyclisations involving the carbamate carbonyl group. Deiodination provides both *trans*- and *cis*-2,5-disubstituted pyrrolidines [**49** and **50**]; the free amine derived from *trans*-2-butyl-5-pentylpyrrolidine **49d** is a component of a fire ant defence pheromone. X-Ray crystallography was carried out for **37f**, **36**, and **37k**.

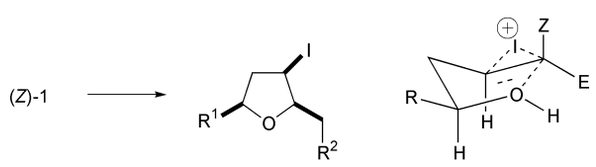
One of the fundamental tenets of Baldwin's rules is that 5-*exo-trig* cyclisations **1** are amongst the most favoured while 5-*endo-trig* processes **2** are the least favoured (Fig. 1).[1] However, it is now well established from results obtained by a number of groups,[2] including ours,[3] that 5-*endo-trig* cyclisations of (*E*)-homoallylic alcohols **3** can be induced using both iodonium and phenylselenenium cations leading to excellent yields of tetrahydrofurans [*e.g.* **4**] (Scheme 1). Such cyclisations are



3 **4**

Scheme 1

usually highly stereoselective, in contrast to similar 5-*exo-trig* cyclisations;[4] (*Z*)-homoallylic alcohols can similarly be converted into the all-*cis*-diastereoisomers **5**, although in poorer



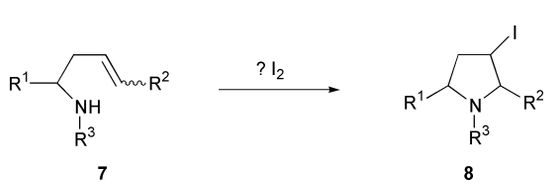
5 **6**

yields.[3] These observations can be explained by the transition state conformation **6** wherein the selective generation of the 2,5-*trans*-iodotetrahydrofurans **4** is controlled by the pseudo-equatorial positioning of the substituent R^1. The necessary 'axial' position which has to be adopted by the alkene substituent (Z) accounts for the poorer yields obtained from simple (*Z*)-homoallylic alcohols, although a suitably positioned hydroxy group results in much higher yields and stereo-

1 **2**

Fig. 1

selection.[5] As electrophile-driven reactions, these cyclisations are not exceptions to Baldwin's rules; indeed, a nucleophilic centre, when positioned such that it can undergo a competing 5-*exo* cyclisation will react preferentially, except in exceptional circumstances.[2,3,6] Further, the additional demands present in such 5-*endo* cyclisations seem to emphasise the requirement for the well-ordered and probably late transition state conformation **6**,[7] of the lowest possible energy, in contrast to the less stereoselective 5-*exo* cyclisations. In the light of the synthetic utility of these reactions, we asked the perhaps obvious question: is it possible to carry out similar cyclisations with homoallylic amine derivatives **7** and thus define a new and equally useful approach to pyrrolidines **8** (Scheme 2)? Herein, we report



7 **8**

Scheme 2

in full that this is indeed possible and describe some of the surprises associated with this chemistry.[8]

Results and discussion

Our first consideration was the nature of the nitrogen protecting group R^3 (Scheme 2). That the amine group required

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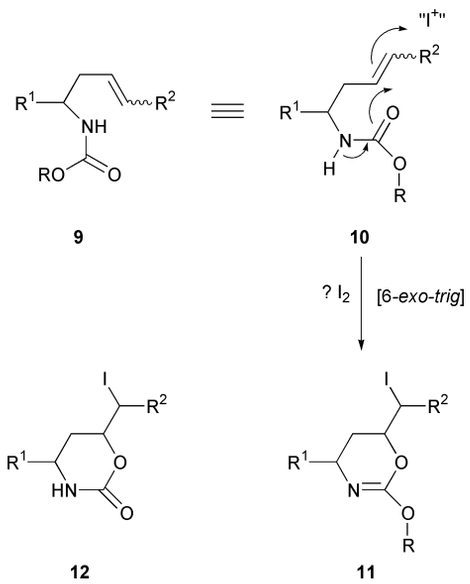
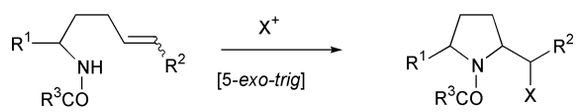
protection seemed plain from studies of the reactions between amines and molecular iodine which result in *N*-iodination, the formation of molecular complexes and, in some cases, unusual oxidation processes.[9] Further, the stability of an iodopyrrolidine with no *N*-protection was an additional point of concern. It seemed unlikely that carbamates or *N*-acyl derivatives would be an optimum choice. The disfavoured nature of 5-*endo*-*trig* cyclisations suggested that such substrates as **9** would



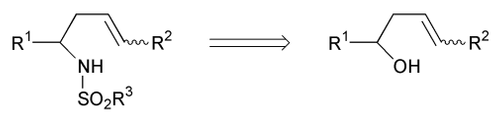
preferentially undergo a 6-*exo* cyclisation (**10**) to give, at least initially, the heterocycles **11**. Alternatively, loss of the carbamate alkyl group, certainly plausible if an *N*-Boc or Cbz group were to be used (*i.e.* R = Bu^t or PhCH$_2$), would lead to the cyclic carbamates **12**, also by a 6-*exo* process. In these considerations, we were guided by previous reports on the 5-*exo*-*trig* cyclisation of pent-4-enamine derivatives **13**, leading to pyrrolidines **14**, and related cyclisations of pent-4-enamides leading, when successful, to the corresponding 5-membered lactams.[4] For example, conversion of pent-4-enamides into the corresponding *N*,*O*-bis(trimethylsilyl) derivatives[10] or thioimidates[11] is necessary for the nitrogen to act as the nucleophile, leading to lactams; similarly, direct iodocyclisation of unsaturated thioamides results in sulfur acting as the nucleophilic centre, leading to tetrahydrothiophene derivatives.[12] However, both *N*-tosyl-3-hydroxypent-4-enamines[13] and related unsaturated *N*-alkoxyamines[14] undergo smooth iodocyclisations while various *N*-acyl derivatives are unreactive,[13] perhaps because of an insufficiently low pK_a value of the N–H bond.[15] Direct 5-*exo* iodocyclisation of an amide is possible in the case of but-3-enyl-β-lactams to give carbapenems, not surprisingly, as the alternative cyclisation *via* oxygen would lead to a rather strained bridged species.[16] Apparent examples of 5-*endo* amide cyclisations in a similar system[17] or ones which lead to β-alkoxypyrrolidines[18] may, in reality, proceed by a 5-*exo* process[6] or by a more complex mechanism, respectively. Similarly, selenocyclisations of unmodified pent-4-enamides tend to result in reaction *via* oxygen rather than nitrogen to give tetrahydrofuran derivatives.[19] However, in contrast, such 5-*exo* cyclisations of carbamates **13**, derived from pent-4-enamines, generally work well to give *N*-alkoxycarbonylpyrrolidines.[20] Although free alkenylamines fail to cyclise smoothly, *ortho*-allylanilines do undergo selenocyclisation efficiently, as exemplified in an elegant approach to the mitomycin skeleton.[21] Similarly, *N*-acetylpent-4-enamines (**13**; R^3 = Me)[22] and the corresponding *N*-pentenylimidates[23] cyclise in a 5-*exo* manner to give selenomethylpyrrolidines. An attempted 5-*endo* selenocyclisation of *N*-acetylbut-3-enamine resulted instead in reaction at oxygen by a 6-*exo* pathway (*cf.* **11**). Mercury(II)-induced 5-*exo* cyclisations seem to be more flexible, as these are possible with both *N*-alkylpent-4-enamines[24,25] and the corresponding carbamates.[26] By careful choice of conditions and reagents, these can be highly stereoselective, giving the 2,5-*trans* diastereoisomers as the kinetic products and the corresponding 2,5-*cis* isomers under thermodynamic conditions. Interestingly, an isolated example of a 5-*endo* cyclisation has been reported: treatment of *N*-propylbut-3-enamine with mercury(II) chloride in tetrahydrofuran gives 3-chloromercurio-1-propylpyrrolidine.[24] A similar mechanism probably operates in the generation of bis-mercuriopyrrolidines by the addition of tosylamine and mercury(II) nitrate to 1,4-dienes leading to β-mercuriopyrrolidines.[27] Direct 5-*exo* sulfenocyclisation of *N*-benzoylpent-4-enamines (**13**; R^3 = Ph)[28] and of *N*-tosyl-2-allylanilines[29] is also viable, given that an activated sulfenium species is employed (Scheme 3). Alternatively, the necessary episulfonium



Scheme 3

species can be generated by a prior mercury(II)-induced cyclisation[30] or by the addition of benzenesulfenyl chloride to an *N*-alkylbut-3-enamine followed by intramolecular displacement of the halogen by sulfur.[31] In this latter example, the overall reaction is a 5-*endo* process. There are also many examples of palladium-induced 5-*exo* cyclisations of these types of amine derivatives (**9**, **13**); an advantage of this methodology is the range of additional substituents which can be incorporated by further reactions of the intermediate palladium species.[32]

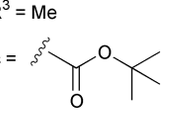
In view of the chemistry outlined above, we chose to use the sulfonamide group for protection of the nitrogen function in our initial studies of the prospects for effecting 5-*endo*-*trig* iodocyclisations of homoallylic amine derivatives, since we expected that it would not participate directly in such reactions. More positively, this functionality had previously been found to be particularly reactive in electrophile-induced cyclisations, presumably because of its ability to lower the pK_a of the N–H bond.[15,33] Thus, we required a series of sulfonamides **15**. As we



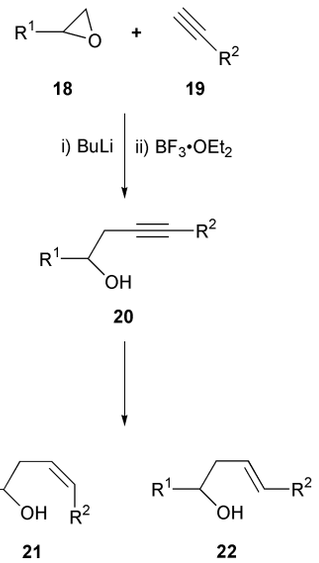
BocNHSO$_2$R^3

a) R^3 = Ph;
b) R^3 = *p*-MeC$_6$H$_4$;
c) R^3 = Me

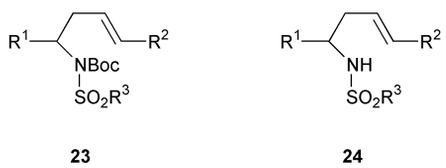
17



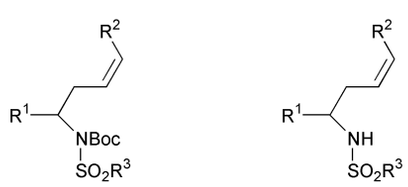
had available proven methodology for the formation of the corresponding homoallylic alcohols **16**,[3,7] an efficient approach to such substrates appeared to be by Mitsunobu reaction[34] between these and the sulfonamide derivatives **17**, as developed by Weinreb and colleagues.[35] As we reported previously,[3,7] the alcohols **16** were readily prepared by sequential Yamaguchi–Hirao condensation[36] between monosubstituted epoxides **18** and acetylenes **19** followed by reduction of the resulting alcohols **20** using various methods to give either the (*Z*)- or (*E*)-homoallylic alcohols **21** or **22** (Scheme 4). In our hands, the Weinreb reagents **17** were easily prepared as previously reported and underwent smooth Mitsunobu reactions with the foregoing



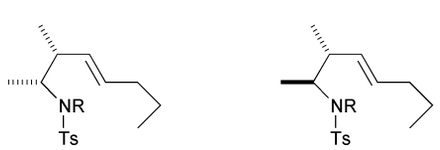
Scheme 4



a) R^1 = Me; R^2 = H; R^3 = Ph;
b) R^1 = H; R^2 = Et; R^3 = *p*-MeC_6H_4;
c) R^1 = H; R^2 = Et; R^3 = Ph;
d) R^1 = Me; R^2 = Bu; R^3 = *p*-MeC_6H_4;
e) as d) but (*R*)-enantiomer;
f) R^1 = Et; R^2 = Bu; R^3 = *p*-MeC_6H_4;
g) R^1 = Et; R^2 = Bu; R^3 = Me;
h) R^1 = Et; R^2 = Pent; R^3 = *p*-MeC_6H_4;
i) R^1 = Bu; R^2 = Pent; R^3 = *p*-MeC_6H_4;
j) R^1 =Et; R^2 = Ph; R^3 = *p*-MeC_6H_4;
k) R^1 = Et; R^2 = Ph; R^3 = Ph.



a) R^1 = H; R^2 = Et; R^3 = *p*-MeC_6H_4;
b) R^1 = H; R^2 = Et; R^3 = Me;
c) R^1 = Et; R^2 = Bu; R^3 = *p*-MeC_6H_4.

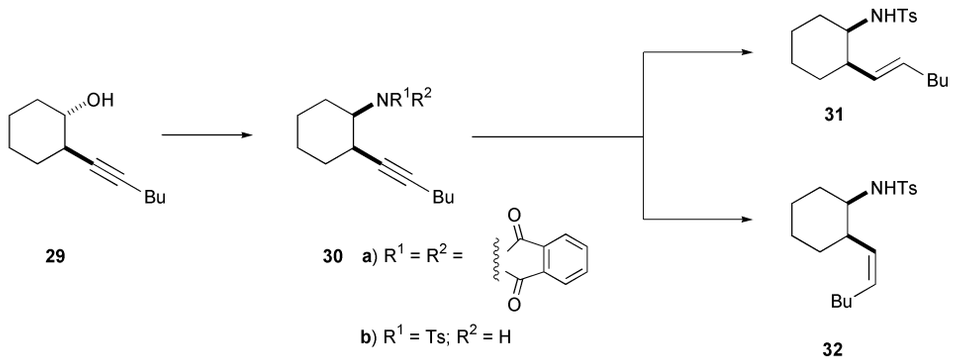


a) R = Boc;
b) R = H.

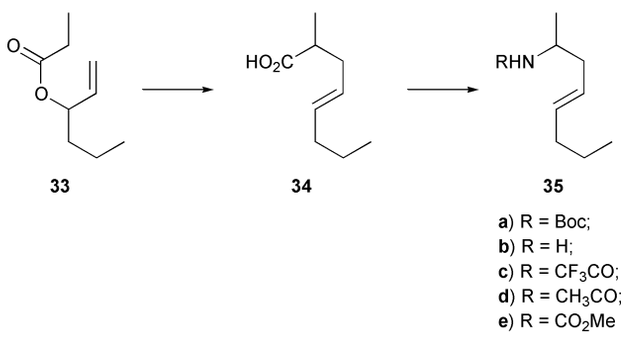
[Ts = *p*-$MeC_6H_4SO_2$]

alcohols to give the expected amine derivatives **23** and **25** in good isolated yields. These were then deprotected using trifluoroacetic acid to give a representative series of precursors **24** and **26**. The more highly substituted analogues **27b** and **28b** were prepared similarly starting from the corresponding epoxybutanes. Condensation between epoxycyclohexane and hex-1-yne provided the cyclohexanol **29**;[7] subsequent Mitsunobu reaction[34] but using phthalimide as the nucleophile gave the expected product **30a** in poor but sufficient yield (Scheme 5). When the *N*-Boc-sulfonamides **17** were used in place of phthalimide, only elimination products were isolated; various azide displacements were similarly unproductive.[37] Protecting group exchange and reductions then gave the required (*E*)- and (*Z*)-isomers **31** and **32**. The preparation of a range of homoallylic amines protected by carbonyl-based groups was achieved by a different approach (Scheme 6): enolate Claisen rearrangement[38] of the ester **33** led smoothly to the unsaturated acid **34**, a modified Curtius rearrangement of which using diphenyl phosphorazidate[39] gave the Boc-protected unsaturated amine **35a**. Deprotection gave the corresponding amine **35b**; standard acylation methods then gave a series of derivatives **35c**–**e**.

In our initial studies, we naturally chose to use the conditions which had been so successful in effecting iodocyclisations of homoallylic alcohols, *i.e.* treatment of the appropriate substrate with three equivalents each of iodine and sodium hydrogen carbonate in dry acetonitrile at ambient temperature. Our first experiment proved the viability of the idea, using the sulfonamide **24a** having no distal substituent. We were pleased to find that cyclisation did occur, although the reaction gave a number of other products and almost no stereoselection (Table 1). Encouraged by this, we next found that the sulfonamide **24b** underwent smooth and rapid cyclisation to give only the *trans*-2,3-iodopyrrolidine **36b**. Similarly the phenylsulfonyl derivative **24c** gave only the iodopyrrolidine **36c** in good yield, a stereoselection which reflects the expected *anti*-addition across the double bond. However, there was distinctly less stereoselection when we attempted to form trisubstituted pyrrolidines under these conditions. Thus, the precursors **24f** and **24j**, while undergoing encouragingly efficient cyclisations, gave synthetically uninteresting mixtures of the products **36f**–**37f** and **36j**–**37j**, in marked contrast to similar cyclisations leading to tetrahydrofurans.[3] Various changes to the conditions including lowering the temperature to 0 °C and even −78 °C and changing the solvent to ether or dichloromethane did not result in any improvement. Fortunately, we observed that the isomer ratio in the products **36f**–**37f** derived from sulfonamide **24f** varied significantly, depending upon the exact method of work up. We wondered if this could be due to the presence of variable amounts of acid arising from the cyclisation itself causing an isomerisation and reasoned that a stronger base might improve matters. To our satisfaction, changing the base from sodium hydrogen carbonate to the slightly stronger potassium carbonate resulted in the almost exclusive formation of the iodopyrrolidine **36f** from the sulfonamide **24f** under conditions otherwise identical to those used initially. Subsequently, this was used as the base throughout and, as summarized in Table 1, all such reactions were highly selective in favour of the 2,5-*trans*-isomers **36**. A surprise associated with this particular recipe was the effect of water. In our previous work on the tetrahydrofuran synthesis, we had deduced that the presence of water was especially deleterious to cyclisation, due to its competing by attacking the iodonium ion intermediate to give the corresponding iodohydrins. However, we discovered that, in marked contrast to this, in the present sulfonamide cyclisations, when potassium carbonate was used as the base, the addition of small amounts of water not only improved the yields but also the stereoselectivity, in favour of isomers **36**. We assume that this is because, under these conditions, the hydrogen iodide produced is more quickly neutralised by the base and hence cannot cause isomerization of these initial products (see below) and that water did not compete as a nucleophile to give iodohydrins.



Scheme 5

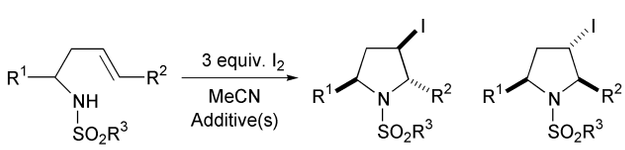


Scheme 6

These results suggested that, in the absence of base, it might be possible to completely isomerize the presumed initial products **36** to the isomers **37**. We were delighted to find that when sulfonamide **24f** was treated with three equivalents of iodine in acetonitrile, an extremely rapid cyclisation occurred from which was isolated only isomer **37f** in excellent yield. The same result was obtained with all of the other arylsulfonamides, as detailed in Table 1. For reasons which are unclear, it was fortunate that we chose this particular protecting group. As shown in Table 1, the corresponding methanesulfonamide **24g** failed to undergo isomerization but instead gave the same product **36g**, no matter whether base was present or not. The more highly substituted isomers **27b** and **28b** also underwent smooth cyclisation to provide good yields of the iodopyrrolidines **38** and **39**, essentially as single isomers, whether or not any base was present. Finally, both the (*E*)- and (*Z*)-alkenyl substituted cyclohexane derivatives **31** and **32** underwent cyclisation simply by the addition of iodine (*i.e.* no base was used) to give the perhydroindole derivatives **40** and **41**, in much the same way as the corresponding octahydrobenzofurans can be formed from alk-2-enylcycloalkanols.[7] However, these last two cyclisations are no more than proof of concept as the yields attained during preparation of the precursors were so poor.

We then turned to an examination of similar iodocyclisations of the related (*Z*)-sulfonamides **26**; the results are summarized in Table 2. As is evident from this Table, such cyclisations were not as successful under any of the conditions tried, both in terms of yields and stereoselection. The products were identified from NMR spectra of the mixtures obtained, by comparisons with pure isomers obtained as indicated in Table 1. These results are very much in line with those obtained from cyclisations of the related (*Z*)-homoallylic alcohols (see below).[3] The results from cyclisations of the trisubstituted pyrrolidine precursor **26c** were unexpected. Conformation **6** suggests that the initial product should be the all-*cis* isomer **44**; however, less of this was isolated under basic conditions than under acidic

Table 1 Iodocyclisations of (*E*)-homoallylic sulfonamides **24**



24 36 37

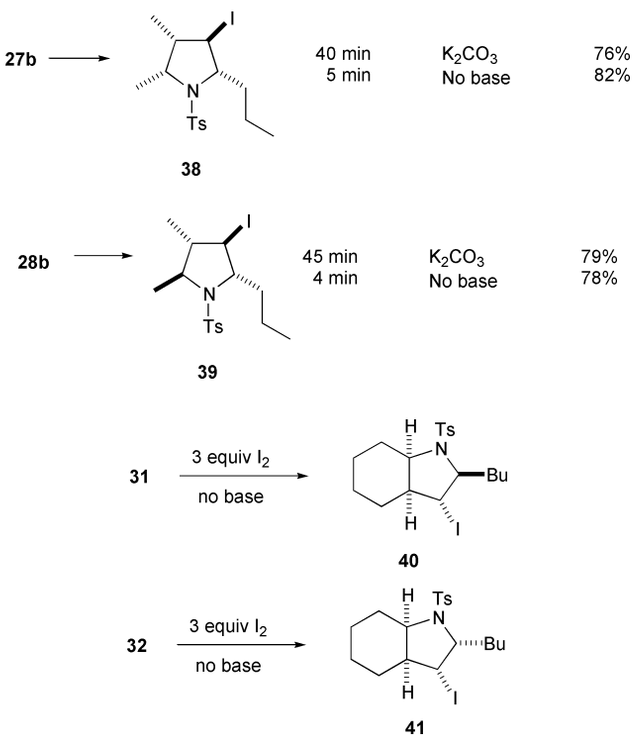
Substrate	R^1	R^2	R^3	Time/min	Additive	Yield (%)	Ratio **36** : **37**
24a	Me	H	Ph	60	$NaHCO_3$	42	60 : 40
24b	H	Et	*p*-Tol	10	$NaHCO_3$	84	100 : 0
				20	K_2CO_3	73	100 : 0
				2	No base	88	100 : 0
24c	H	Et	Ph	10	$NaHCO_3$	84	100 : 0
24d	Me	Bu	*p*-Tol	25	K_2CO_3	85	93 : 7
				3	No base	86	0 : 100
24e [(*R*)-**24d**]				3	No base	85	0 : 100
24f	Et	Bu	*p*-Tol	25	$NaHCO_3$	76	74 : 26
				30	K_2CO_3	74	94 : 6
				3	No base	78	0 : 100
24g	Et	Bu	Me	25	K_2CO_3	72	97 : 3
				3	No base	78	94 : 6
24h	Et	Pent	*p*-Tol	25	K_2CO_3	79	97 : 3
				3	No base	74	0 : 100
24i	Bu	Pent	*p*-Tol	35	K_2CO_3	78	94 : 6
				15	No base	76	0 : 100
24j	Et	Ph	*p*-Tol	40	$NaHCO_3$	76	65 : 35
				45	K_2CO_3	83	94 : 6
				10	No base	76	0 : 100
24k	Et	Ph	Ph	10	No base	81	0 : 100

conditions, when isomerization was expected, suggesting that perhaps an alternative conformation is involved.

The final group of substrates examined were the series of (*E*)-*N*-acyl derivatives **35**, which we expected to undergo competing 6-*exo* cyclisation to at least some degree, if not completely (see above; structures **9** to **12**). In the event (Table 3), only small amounts (10%) of the desired pyrrolidines **47** and **48** were formed in all cases. These were identified by comparisons with foregoing compounds (Table 1). The major products were tentatively identified as those from 6-*exo* cyclisations. In the case of the *N*-Boc derivative **35a**, loss of the *tert*-butyl group was evident; other NMR data on the 2 : 1 mixture of isomers obtained were consistent with the cyclic carbamate structures **45**, epimeric at the methyl substituent, given the expected *anti*-addition across the double bond. Although this cyclisation is reasonably efficient, the relative lack of stereoselection rather detracts from any synthetic utility. Not surprisingly, under acidic conditions, some of the starting amine **35b** was also obtained. Similar cyclisations of the acetyl and trifluoroacetyl derivatives **35c** and **35d** gave the alternative 6-*exo* products **46c,d**, as unstable mixtures of isomers which again were not fully characterized. This latter mode of cyclisation also appeared to occur with the methoxycarbonyl derivative **35e**, presumably because loss of a methyl carbocation is much less favourable than loss of *tert*-butyl. Overall, most of these cyclisations gave mixtures of a number of compounds and are certainly not synthetically useful, at least under the present sets of conditions.

Finally, we briefly examined some reactions of the initial products **36** and **37**. Firstly, deiodination using tributyltin hydride led smoothly to the expected 2,5-disubstituted pyrrolidines **49** and **50** in good yields. In no cases was any isomerization observed. A number of such 2,5-dialkylpyrrolidines, with combinations of C_2, C_4, C_6 and C_7 side chains, have been identified as components in the defence secretions of various fire ants.[40] A specific example is the free amine derived from the *trans*-5-butyl-2-pentylpyrrolidine **49d** which has previously been synthesized by low yielding and non-stereoselective approaches, in which a final step is removal of the *N*-tolylsulfonyl group using lithium aluminium hydride.[41] This present chemistry therefore could be used to selectively prepare both possible diastereoisomers of such structures and to obtain optically pure samples. It also proved possible to effect base-induced E_2 eliminations of the initial products to provide access to the corresponding 3-pyrrolines **51** and **52**; again, no isomerization occurred in the two examples examined.

Throughout these studies, the structures of the various isomeric pyrrolidines were determined in much the same way as in our work on tetrahydrofuran synthesis.[3] Firstly, CHI functions were identified in ^{13}C spectra from their unique position around 20–30 ppm, due to the heavy atom effect.[42] Subsequent ^1H–^1H and ^1H–^{13}C correlation experiments then allowed full assignment of each resonance and crucially confirmed that the products were indeed pyrrolidines and not azetidines which could arise from 4-*exo*-*trig* cyclisations. As is typical of five-membered rings, coupling constant data were not helpful in determining stereochemistry. In some examples (**36f**, **36j**), the problem of overlapping resonances was solved by running the ^1H NMR spectra in solvents other than deuteriochloroform. However, NOE measurements gave reasonable indications of the assigned stereochemistries, but were certainly not definitive, as was the case with the related tetrahydrofurans.[3] Definite structural proof was finally achieved by pertinent literature comparisons, especially of ^1H NMR data[43] and, in particular, by single crystal X-ray determinations of the *cis*-2,5-dialkyl-3-iodopyrrolidine **37f** together with the isomeric 2-phenylpyrrolidines **36j** and **37k**.[44] Although many of the iodopyrrolidines were obtained as solids, these did not provide crystals suitable for X-ray analysis from the initial recrystallisations. Suitable samples were eventually obtained by a vapour



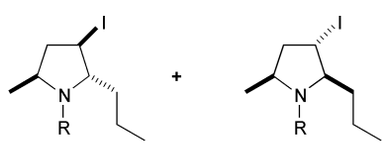
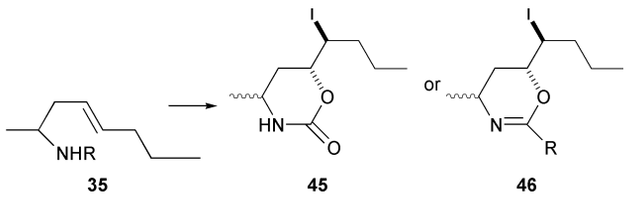


Table 2 Iodocyclisations of (*Z*)-homoallylic sulfonamides **26**

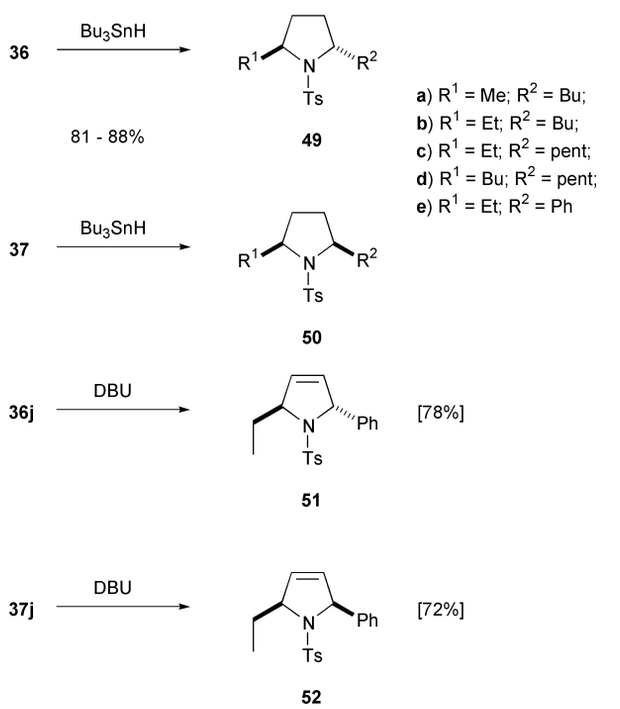
		R	Time/min	Base	Yield (%)	Product ratio
26a,b → **42** + **43**		R = Ts	60	$NaHCO_3$	40	**42a** : **43a** [**36b**] = 35 : 65
			60	K_2CO_3	52	**42a** : **43a** [**36b**] = 38 : 62
			60	No base	35	Gross mixture
		R = Me	60	$NaHCO_3$	45	**42b** : **43b** = 50 : 50
			24 h	K_2CO_3	~0	
			60	No base	40	Gross mixture
26c → **44** + **36f** + **37f**			60	$NaHCO_3$	65	**44** : **36f** : **37f** = 43 : 30 : 27
			60	K_2CO_3	63	**44** : **36f** : **37f** = 27 : 83 : ~0
			60	No base	57	**44** : **36f** : **37f** = 66 : 19 : 15

Table 3 Iodocyclisations of homoallylic carbamates and amides **35**



35 **45** **46**

R	Time/min	Base	Yield (%)	Product ratio
a) R = Boc	30	K_2CO_3	79	**45** (66 : 34)
	30	No base	67	**45** (67 : 35) [+15% of amine **35b**]
c) R = CF_3CO	60	K_2CO_3	57	**46c** (76 : 24) [R = CF_3]
	60	No base	—	Gross mixture
d) R = CO_2Me	60	K_2CO_3	0	No reaction
	60	No base	67	**46d** (76 : 24) [R = Me]
e) R = CO_2Me	60	K_2CO_3	48	**46e** (66 : 34) [R = OMe]
	60	No base	42	**46e** (66 : 34)



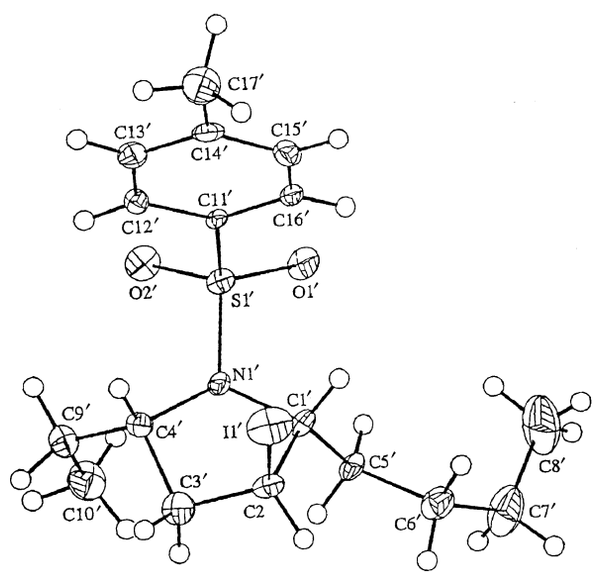


Fig. 2 (2*RS*,3*SR*,5*SR*)-2-Butyl-5-ethyl-3-iodo-1-*p*-tolylsulfonylpyrrolidine **37f**.

diffusion method in which a concentrated ethereal solution of the particular iodopyrrolidine was stored for up to one month in an atmosphere of hexane at ambient temperature. The crystal structure determinations of the iodopyrrolidines **37f** and **36j** proceeded uneventfully and confirmed the respective 2,5-*cis* and 2,5-*trans* stereochemical assignments made on the basis of NMR data; these are shown in Figs. 2 and 3. However, the vapour diffusion crystallisation of iodopyrrolidine **37k** provided an unexpected complication: on close inspection of the sample, two crystalline forms were apparent, one as orange clusters (mp 103–104 °C) while the other, minor, component (mp 95–97 °C) appeared as colourless rectangles. Fearing either decomposition of the sample or, worse, an unexpected isomerisation, individual samples were separated by hand and both were subjected to X-ray analysis. We were surprised and delighted to find that *both* confirmed the assigned 2,5-*cis* stereochemistry of compound **37k** and that the two crystal forms were in fact differing conformations of the same diastereoisomer. The major and minor structures observed, **37k(i)** and **37k(ii)**, are presented in Figs. 4 and 5 respectively. In the major conformation, the phenyl and iodine substituents appear in pseudoequatorial positions with the ethyl group positioned pseudoaxially and the arylsulfonyl group *trans* to both α-substituents. This more stable conformation contrasts with the minor diastereoisomer (Fig. 5) in which the iodine appears to be pseudoaxial. Subsequently, we observed, as expected, that samples of the minor conformation **37k(ii)** exhibited spectroscopic data (infra-red, ^{1}H and ^{13}C NMR) in solution which were identical to those displayed by the bulk sample of compound **37k**. Despite this amusing complication, comparisons of the spectral data displayed by these three compounds with all the other products then completed the structural assignments.

It therefore seemed most likely that the *trans*-2,5-disubstituted pyrrolidines **36** obtained from cyclisations under basic conditions were the kinetic products and that these were isomerized under acidic conditions to the thermodynamically more stable *cis*-2,5-disubstituted pyrrolidines **37**.[45] There was, however, a final structural problem associated with this idea: the *trans*-disposition of the 2-substituent and the 3-iodo group in the 2,5-*cis*-stereoisomers **37** strongly suggested that isomerization of the initial *trans*-isomers **36** was occurring by ring opening and reclosure. However, it was possible that, in some way, the 5-centre in isomers **36** was undergoing epimerization to give the more stable *cis*-isomers **37**. As the two possible structures are enantiomeric [*i.e.* **37** or **36** with R^1 'down' or α-], we were unable to distinguish these two pathways using the foregoing

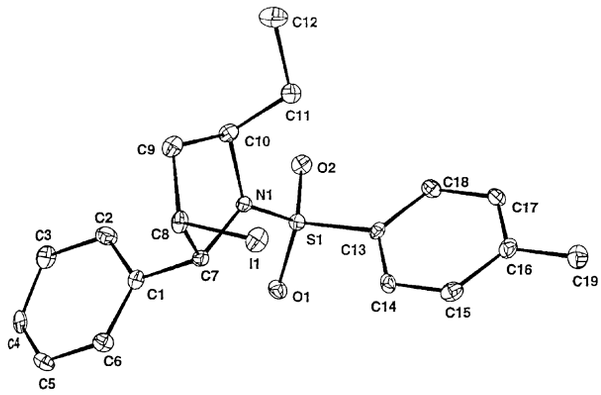


Fig. 3 (2*RS*,3*SR*,5*RS*)-5-Ethyl-3-iodo-2-phenyl-1-*p*-tolylsulfonylpyrrolidine **36j**.

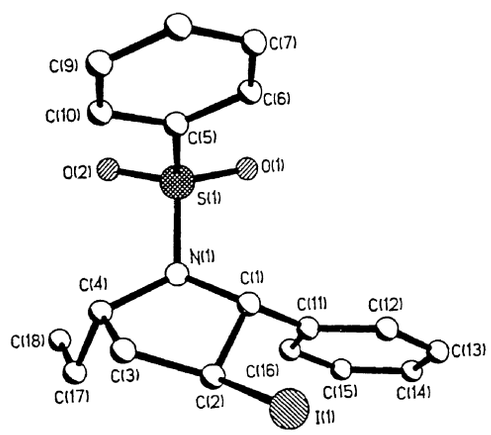


Fig. 4 (2*RS*,3*SR*,5*SR*)-5-Ethyl-3-iodo-2-phenyl-1-phenylsulfonylpyrrolidine **37k(i)**.

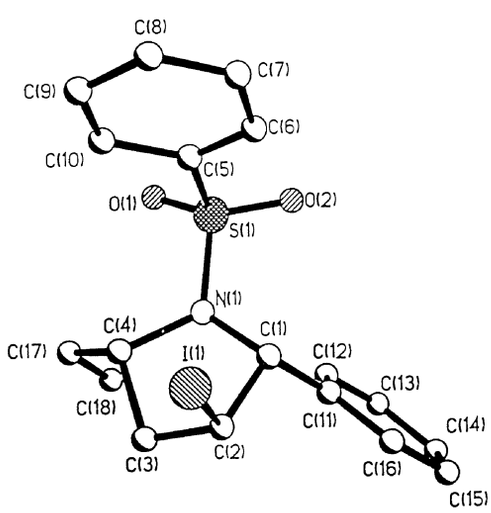
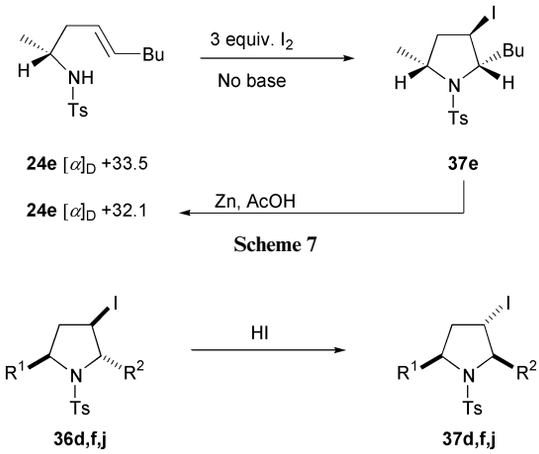


Fig. 5 (2*RS*,3*SR*,5*SR*)-5-Ethyl-3-iodo-2-phenyl-1-phenylsulfonylpyrrolidine **37k(ii)**.

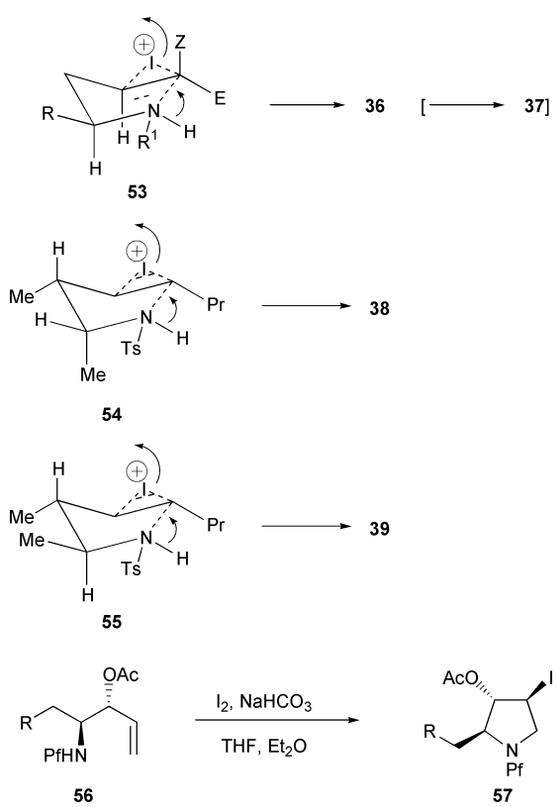
racemates. We therefore prepared the enantiopure homoallylic sulfonamide **24e** [(*R*)-**24d**], starting from (*S*)-epoxypropane, and subjected this to cyclisation under acidic conditions and isolated the expected iodopyrrolidine **37e**. Cycloreversion by deiodination using zinc metal in acetic acid then provided the starting sulfonamide **24e** with essentially the same optical rotation (Scheme 7). As confirmation of this, we found that selected examples of the *trans*-stereoisomers **36d**,**f**,**j** underwent isomerization to the corresponding *cis*-isomers **37d**,**f**,**j** when exposed to hydrogen iodide; other acids such as sulfuric acid and trifluoroacetic acid did not cause isomerization although exposure to 6 M hydrochloric acid resulted in partial isomerization (Scheme 8). Hence, we conclude that isomerization does indeed occur by cycloreversion and recyclisation and not by epimerization at the 5-position.



Scheme 7

Scheme 8

The formation of the *trans*-pyrrolidines **36** as kinetic products can be understood by the chair-like conformation **53**, in which the substituent R is positioned equatorially, along much the same lines as that proposed (**6**) for the related tetrahydrofuran synthesis; the pseudoaxial position of the substituent 'Z' in such a conformation presumably accounts for the poor returns from cyclisations of the (*Z*)-homoallylic sulfonamides **26**. The tetrasubstituted iodopyrrolidines **38** and **39**



Scheme 9

were resistant to isomerisation. This was not surprising, as a similar conformation **54** would lead to the *cis*-isomer **38** from the *anti*-sulfonamide **27b** which would not gain from such an isomerisation to a less thermodynamically stable 2,5-*trans*-pyrrolidine. The *syn*-isomer **28b** presumably undergoes cyclisation *via* conformation **55** in which all substituents are effectively equatorial to give a product **39** in which each substituent has a *trans* relationship to the adjacent groups, thus

presumably overcoming any advantage associated with a 2,5-*cis* stereochemistry. These considerations should be useful in synthetic design in this area. A limitation of the present method is that this type of cyclisation, when applied to homoallylic sulfonamides having a terminal alkene function (**24a**), gives a poor yield of a mixture of isomers (**36a** and **37b**). After completion of these studies, a possible solution to this was reported in similar iodocyclisations, but of *N*-9-phenylfluorenyl homoallylic amines **56**, which give good yields of the pyrrolidines **57**.[46] However, the presence of an allylic acetate group may also assist these cyclisations.[5]

In summary, this application of the 5-*endo*-*trig* method has provided a flexible approach to both *trans*- and *cis*-2,5-disubstituted pyrrolidines. Optically pure pyrrolidines will be obtained by starting with single enantiomers of the homoallylic alcohols **22**, as demonstrated in the preparation of the iodopyrrolidine **37e**, at least in examples such as this where there is no opportunity for racemization. One limitation of this present chemistry is the lack of functionality present in the substituents. In preliminary studies, we have partly addressed this deficiency by demonstrating that sulfonamides derived from α-allylated glycine esters undergo similarly efficient and flexible iodocyclisations to provide examples of substituted prolines in a highly stereoselective manner.[47] Similarly, selenocyclisations of homoallylic sulfonamides **24** are also highly stereoselective, although a variety of conditions have to be employed to achieve this.[48] No doubt many other side-chain substituents will be compatible with the foregoing chemistry. Exceptions may well be when heteroatoms are present in positions in which these can undergo competing 5-*exo* cyclisations as, despite the facile nature of the cyclisations described in this paper, Baldwin's rules are likely to apply in such competitive situations.

Experimental

General details

Melting points were determined on a Köfler hot stage apparatus. Optical rotations were measured using an Optical Activity AA-10 polarimeter and are given in 10^{-1} deg cm^2 g^{-1}. Infrared spectra were recorded using a Perkin-Elmer 1600 series Fourier transform spectrometer using thin films between sodium chloride plates, unless otherwise stated. ^{1}H NMR spectra were determined using a Bruker WM-250, a JEOL EX-270 or a Bruker AM-400 spectrometer, operating at the frequencies indicated [*i.e.* (250) refers to 250 MHz *etc.*]. ^{13}C NMR spectra were determined using any of the latter three instruments, operating at 62.5, 67.8 and 100.1 MHz respectively, as indicated after δ_C. Unless otherwise stated, all spectra were determined using dilute solutions in deuteriochloroform and tetramethylsilane as internal standard. *J* Values are expressed in hertz. Mass spectra were measured using either an AEI MS902 or a VG 7070E instrument, both operating in the electron impact mode, unless otherwise stated; FAB, electrospray (ES) and atmospheric pressure chemical ionization (APcI) spectra were obtained using the latter instrument or were obtained from the EPSRC Mass Spectrometry Service at UC Swansea.

Unless otherwise stated, all reactions were carried out in anhydrous solvents which were obtained by the usual methods.[49] All organic solutions from work-ups were dried by brief exposure to anhydrous magnesium sulfate followed by filtration. Solvents were removed by rotary evaporation. CC refers to column chromatography over Sorbsil silica gel using the eluants specified.

The Mitsunobu reagents **17** were prepared in similar yields to those previously reported and showed identical spectroscopic and analytical data: *N*-*tert*-butoxycarbonylbenzenesulfonamide **17a**, mp 94–95 °C (lit.[50] mp 93–95 °C); *N*-*tert*-butoxycarbonyltoluene-*p*-sulfonamide **17b**, mp 116–117 °C (lit.[35] mp 115–117 °C); *N*-*tert*-butoxycarbonylmethanesulfonamide **17c**, mp 106–107 °C (lit.[51] mp 108–109 °C).

Mitsunobu reactions: general procedure

To a stirred solution of an alkenol **21** or **22** (10 mmol, 1 eq.), a Mitsunobu sulfonamide reagent **17** (10 mmol, 1 eq.) and triphenylphosphine (11 mmol, 1.1 eq.) in dry tetrahydrofuran (60 ml) cooled in an ice-bath was added dropwise diethyl azodicarboxylate (11 mmol, 1.1 eq.). The reaction mixture was stirred at ambient temperature for 6 h then treated with water (50 ml) and extracted with dichloromethane (3 × 50 ml). The combined organic extracts were dried and evaporated to leave the crude product **23, 25, 27a** or **28a** which was either purified by column chromatography (cc) or deprotected without further purification (see later).

4-[(*N*-*tert*-Butoxycarbonylphenyl)sulfonylamino]pent-1-ene 23a. A solution of pent-4-en-2-ol (0.50 g, 5.8 mmol) was reacted with Mitsunobu reagent **17a** (1.50 g, 5.8 mmol) as described in the general procedure to yield a yellow semi-solid which was purified by cc (hexane–ethyl acetate 50 : 50) to afford the *title compound* **23a** (1.40 g, 74%) as a viscous, pale yellow oil: R_f 0.76 (hexane–ethyl acetate 50 : 50); ν_{max}/cm^{-1} 2956 (s), 2940 (s), 2880 (s), 1732 (C=O), 1456 (s) and 1363 (s); δ_H (250) 7.93–7.42 (5H, m, Ph), 5.72 (1H, dddd, *J* 15.8, 12.2, 6.3 and 6.3, 2-H), 5.10–4.96 (2H, m, 1-CH$_2$), 4.64–4.58 (1H, m, 4-H), 2.79–2.40 (2H, m, 3-CH$_2$), 1.47 (3H, d, *J* 8.3, 5-Me) and 1.32 (9H, s, ^{t}Bu); δ_C (67.8) 150.4 (C=O), 140.8 (Ar-C), 135.1 (Ar-CH), 132.6 (2-CH), 128.6 (Ar-CH), 127.7 (Ar-CH), 117.6 (1-CH$_2$), 84.0 (^{t}Bu-C), 54.9 (4-CH), 39.3 (3-CH$_2$), 27.8 (^{t}Bu-Me) and 19.4 (5-Me); *m*/*z* (EI) 284 (M$^+$ − C$_3$H$_5$, 30%), 198 (4), 184 (100), 141 (61), 77 (65) and 57 (98).

(*E*)-3-[(*N*-*tert*-Butoxycarbonyl)-*p*-tolylsulfonylamino]dec-5-ene 23f. (*E*)-Dec-5-en-3-ol (0.66 g, 4.20 mmol) was reacted with Mitsunobu reagent **17b** (1.13 g, 4.20 mmol) as described in the general procedure to give a yellow solid which was purified by cc (dichloromethane) to afford the *title compound* **23f** (1.20 g, 74%) as a pale yellow, viscous oil: R_f 0.68 (dichloromethane); ν_{max}/cm^{-1} 2964 (s), 2930 (s), 2874 (w), 1726 (C=O), 1589 (w), 1458 (s) and 1357 (s); δ_H (400) 7.83 (2H, d, *J* 8.4, Ar-H), 7.26 (2H, d, *J* 8.4, Ar-H), 5.50 (1H, dt, *J* 15.2 and 6.2, 6-H), 5.37 (1H, dt, *J* 15.2 and 6.3, 5-H), 4.34 (1H, tt, *J* 7.3 and 6.3, 3-H), 2.61–2.37 (2H, m, 4-CH$_2$), 2.42 (3H, s, Ar-Me), 1.98–1.72 (4H, m, 2- and 7-CH$_2$), 1.40–1.11 (4H, m, 8- and 9-CH$_2$), 1.38 (9H, s, ^{t}Bu), 0.96 (3H, t, *J* 7.3, 1-Me) and 0.87 (3H, t, *J* 6.8, 10-Me); δ_C (100) 150.7 (C=O), 143.6, 137.7 (both Ar-C), 133.5 (=CH), 128.8, 128.3 (both Ar-CH), 126.5 (=CH), 83.5 (^{t}Bu-C), 65.3 (3-CH), 36.6, 32.2, 31.4 (all CH$_2$), 27.9 (^{t}Bu-Me), 26.3, 22.2 (both CH$_2$), 21.4 (Ar-Me), 13.9 (10-Me) and 11.5 (13-Me); *m*/*z* (EI) 336 (M$^+$ − C$_4$H$_9$O, 3%), 312 (2), 254 (18), 212 (100), 156 (4), 138 (13) and 91 (38) [Found: M$^+$ − C$_4$H$_9$O, 336.1635. C$_{18}$H$_{26}$NO$_3$S requires *M*, 336.1633].

(*E*)-3-[(*N*-*tert*-Butoxycarbonyl)methylsulfonylamino]dec-5-ene 23g. (*E*)-Dec-5-en-3-ol (0.10 g, 0.65 mmol) was reacted with Mitsunobu reagent **17c** (0.13 g, 0.65 mmol) as described in the general procedure to give a crude product as a yellow, semi-solid which was purified by cc (dichloromethane) to afford the *title compound* **23g** (0.16 g, 76%) as a pale yellow, viscous oil: R_f 0.43 (dichloromethane); ν_{max}/cm^{-1} 2965 (s), 2932 (s), 2875 (w), 1724 (C=O), 1459 (w), 1395 (w) and 1353 (s); δ_H (400) 5.46 (1H, dt, *J* 15.3 and 6.7, 6-H), 5.32 (1H, dt, *J* 15.3 and 6.6, 5-H), 4.18 (1H, tt, *J* 7.2 and 6.3, 3-H), 3.21 (3H, s, SO$_2$Me), 2.61–2.58 (1H, m, 4-H$_\alpha$), 2.32–2.21 (1H, m, 4-H$_\beta$), 1.98–1.89 (4H, m, 2- and 7-CH$_2$), 1.65–1.54 (2H, m, 8-CH$_2$), 1.53 (9H, s, ^{t}Bu), 1.30 (2H, m, 9-CH$_2$), 0.92 (3H, t, *J* 7.4, 1-Me) and 0.86 (3H, t, *J* 7.1, 10-Me); δ_C (67.8) 133.8, 126.6 (both =CH), 83.9 (^{t}Bu-C), 61.2 (3-CH), 42.1 (SO$_2$Me), 36.4, 32.2, 31.4 (all CH$_2$), 28.0 (^{t}Bu-Me),

26.3, 22.1 (both CH_2), 13.8 (10-Me) and 11.3 (1-Me); *m*/*z* (FAB) 334 ($M^+ + 1$, 12%), 298 (54), 278 (100), 234 (18), 154 (20), 136 (47), 126 (10), 83 (35), 57 (90) and 55 (20) [Found: $M^+ + 1$, 334.2056. $C_{16}H_{32}NO_4S$ requires *M*, 334.2052].

(*E*)-5-[(*N*-*tert*-Butoxycarbonyl)-*p*-tolylsulfonylamino]tridec-7-ene 23i. (*E*)-Tridec-7-en-5-ol (1.90 g, 9.60 mmol) was reacted with Mitsunobu reagent **17b** (2.60 g, 9.60 mmol) under the general conditions to give a crude product as a yellow semi-solid which was purified by cc (hexane–ethyl acetate 80 : 20) to yield the *title compound* **23i** (3.20 g, 71%) as a colourless, viscous oil: R_f 0.66 (hexane–ethyl acetate 80 : 20); ν_{max}/cm^{-1} 2957 (s), 2929 (s), 2860 (w), 1726 (C=O), 1598 (w), 1356 (s) and 1278 (s); δ_H (400) 7.83 (2H, d, *J* 8.2, Ar-H), 7.28 (2H, d, *J* 8.2, Ar-H), 5.43 (1H, dt, *J* 15.3 and 6.8, 8-H), 5.35 (1H, dt, *J* 15.3 and 6.6, 7-H), 4.48–4.30 (1H, m, 5-H), 2.64–2.37 (2H, m, 6-CH_2), 2.43 (3H, s, Ar-Me), 1.98–1.65 (4H, m, 4- and 9-CH_2), 1.38 (9H, s, ^{t}Bu), 1.34–1.21 (10H, m, 2-, 3-, 10-, 11- and 12-CH_2), 0.82 (3H, t, *J* 6.8, Me) and 0.79 (3H, t, *J* 7.0, Me); δ_C (100) 151.3 (C=O), 143.8 (Ar-C), 137.8 (Ar-C), 133.7 (=CH), 128.9 (Ar-CH), 128.4 (Ar-CH), 126.7 (=CH), 83.7 (^{t}Bu-C), 60.1 (5-CH), 36.9, 33.7, 33.1, 32.6, 29.1 (all CH_2), 28.0 (^{t}Bu-Me), 26.8, 22.5 (both CH_2), 21.53 (Ar-Me) and 13.9 (1- and 13-Me); *m*/*z* (ES) 452 ($M^+ + 1$, 23%), 396 (91), 356 (100) and 245 (34).

(*E*)-4-[(*N*-*tert*-Butoxycarbonyl)-*p*-tolylsulfonylamino]-1-phenylhex-1-ene 23j. (*E*)-1-Phenylhex-1-en-4-ol (3.00 g, 17.00 mmol) was reacted with Mitsunobu reagent **17b** (4.62 g, 17.00 mmol) under the conditions described in the general procedure to give the crude product as a yellow semi-solid which was purified by cc (hexane–ethyl acetate 80 : 20) to afford the *title compound* **23j** (5.60 g, 81%) as a colourless solid, mp 106–107 °C: R_f 0.51 (hexane–ethyl acetate 80 : 20); ν_{max}/cm^{-1} ($CHCl_3$) 2962 (s), 2930 (s), 2862 (s), 1727 (C=O) and 1462 (s); δ_H (250) 7.74 (2H, d, *J* 8.4, Ar-H), 7.33–7.19 (5H, m, Ph), 6.99 (2H, d, *J* 8.4, Ar-H), 6.39 (1H, d, *J* 15.7, 1-H), 6.10 (1H, ddd, *J* 15.7, 7.5 and 6.8, 2-H), 4.50 (1H, tdd, *J* 6.2, 6.2 and 6.1, 4-H), 2.89 (1H, ddd, *J* 14.0, 7.5 and 6.2, 3-H_α), 2.62 (1H, ddd, *J* 14.0, 6.8 and 6.1, 3-H_β), 2.31 (3H, s, Ar-Me), 2.10–1.55 (2H, m, 5-CH_2), 1.38 (9H, s, ^{t}Bu) and 1.01 (3H, t, *J* 7.7, 6-Me); δ_C (100) 150.9 (C=O), 143.6, 137.5, 136.9 (all Ar-C), 132.7 (Ar-CH), 128.9 (=CH), 128.4, 128.3, 127.3, 127.14 (all Ar-CH), 126.2 (=CH), 83.9 (^{t}Bu-C), 61.3 (4-CH), 36.9 (3-CH_2), 28.0 (^{t}Bu-Me), 26.9 (5-CH_2), 21.5 (Ar-Me) and 11.5 (6-Me); *m*/*z* (ES) 430 ($M^+ + 1$, 100%), 374 (92), 330 (84), 83 (28) and 60 (52) [Found: C, 66.9; H, 7.4; N, 3.2. $C_{24}H_{31}NO_4S$ requires C, 67.1; H, 7.3; N, 3.2%].

(*Z*)-1-[(*N*-*tert*-Butoxycarbonyl)-*p*-tolylsulfonylamino]hex-3-ene 25a. (*Z*)-Hex-3-en-1-ol (0.50 g, 5.0 mmol) was reacted with Mitsunobu reagent **17b** (1.35 g, 5.0 mmol) as described above to give an orange semi-solid which was purified by cc (dichloromethane) to yield the *title compound* **25a** (1.30 g, 74%) as a viscous, pale yellow oil: R_f 0.62 (dichloromethane); ν_{max}/cm^{-1} 3307 (w), 2969 (s), 2933 (s), 1728 (C=O), 1356 (s) and 1289 (s); δ_H (400) 7.79 (2H, d, *J* 8.2, Ar-H), 7.29 (2H, d, *J* 8.2, Ar-H), 5.51–5.29 (2H, m, 3- and 4-H), 3.86–3.79 (2H, m, 1-CH_2), 2.62–2.45 (2H, m, 2-CH_2), 2.44 (3H, s, Ar-Me), 2.11 (2H, qd, *J* 7.5 and 7.4, 5-CH_2) 1.35 (9H, s, ^{t}Bu) and 0.98 (3H, t, *J* 7.5, 6-Me); δ_C (100) 151.0 (C=O), 144.0, 137.7 (both Ar-C), 134.8 (=CH), 129.2, 127.8 (both Ar-CH), 124.1 (=CH), 84.0 (^{t}Bu-C), 46.6 (1-CH_2), 28.2 (CH_2), 27.9 (^{t}Bu-Me), 21.5 (Ar-Me), 20.6 (CH_2) and 14.2 (6-Me); *m*/*z* (FAB) 354 ($M^+ + 1$, 36%), 298 (100), 280 (7), 254 (17), 184 (13), 155 (33), 139 (10), 126 (30), 91 (17), 82 (13) and 57 (32) [Found: $M^+ + 1$, 354.1749. $C_{18}H_{28}NO_4S$ requires *M*, 354.1739].

(*Z*)-1-[(*N*-*tert*-Butoxycarbonyl)methylsulfonylamino]hex-3-ene 25b. (*Z*)-Hex-3-en-1-ol (0.10 g, 1.0 mmol) was reacted with Mitsunobu reagent **17c** (0.19 g, 1.0 mmol) as described in the general procedure to give a dark yellow semi-solid which was purified by cc (dichloromethane) to yield the *title compound* **25b** (0.20 g, 80%) as a thick, pale yellow oil: R_f 0.52 (dichloromethane); ν_{max}/cm^{-1} 3008 (w), 2973 (s), 2935 (s), 2875 (w), 1726 (C=O), 1487 (w) and 1355 (s); δ_H (400) 5.48–5.29 (2H, m, 3- and 4-H), 3.69 (2H, t, *J* 7.3, 1-CH_2), 3.26 (3H, s, SO_2Me), 2.37 (2H, td, *J* 7.3 and 7.2, 2-CH_2), 2.05 (2H, qd, *J* 7.5 and 7.3, 5-CH_2), 1.54 (9H, s, ^{t}Bu) and 0.95 (3H, t, *J* 7.5, 6-Me); δ_C (100) 151.6 (C=O), 134.6, 124.1 (both =CH), 84.1 (^{t}Bu-C), 45.6 (1-CH_2), 42.0 (SO_2Me), 27.8 (^{t}Bu-Me), 27.4, 20.3 (both CH_2) and 14.0 (6-Me); *m*/*z* (FAB) 278 ($M^+ + 1$, 36%), 222 (100), 204 (9), 178 (33), 154 (44), 137 (41), 83 (23) and 57 (73) [Found: $M^+ + 1$, 278.1429. $C_{12}H_{24}NO_4S$ requires *M*, 278.1426].

(1*RS*,2*RS*)-2-(Hex-1-ynyl)-1-phthalimidocyclohexane 30a. A solution of phthalimide (5.20 g, 36.0 mmol) and triphenylphosphine (9.40 g, 36.0 mmol) in dry THF (100 ml) was stirred under nitrogen at ambient temperature. To this was added alkynol **29** (2.16 g, 12 mmol)[7] and diethyl azodicarboxylate (5 ml, 36.0 mmol). Stirring was continued for 48 h, after which time the solvent was evaporated and the crude product purified by cc (hexane–ether 80 : 20) to furnish the *phthalimide* **30a** (1.50 g, 46%) as a viscous oil: ν_{max}/cm^{-1} 1772 (C=O), 1714 (C=O) and 1330; δ_H (400) 7.85–7.78 (2H, m, Ar-H), 7.73–7.67 (2H, m, Ar-H), 4.11 (1H, dt, *J* 13.0 and 3.6, 1-H), 3.53–3.02 (1H, m), 2.09 (2H, td, *J* 7.0 and 2.3, 3′-CH_2), 1.97–1.22 (10H, m) and 0.90 (3H, t, *J* 7.2, Me); δ_C (67.8) 168.5 (Ar-C), 133.6, 122.8 (both Ar-CH), 83.5, 79.2 (both C), 55.4, 33.0 (both CH), 31.1, 26.3, 24.9, 22.1, 20.9, 20.7 (all CH_2) and 13.40 (Me); *m*/*z* (ES) 310 ($M^+ + 1$, 100%), 151 (24) and 134 (51) [Found: $M^+ + 1$, 310.1807. $C_{20}H_{24}NO_2$ requires *M*, 310.1806].

Boc deprotections: general procedure

To a stirred solution of an *N*-Boc-arene (or alkane) sulfonamide (10.0 mmol, 1 eq.) in dichloromethane (50 ml) was added dropwise trifluoroacetic acid (11.4 ml, 100 mmol, 10 eq.). The resulting mixture was stirred at ambient temperature, typically for 10–20 h. Once the reaction was complete, the mixture was neutralised using 2 M aqueous sodium carbonate and the resulting two layers separated. The aqueous layer was extracted with dichloromethane (3 × 50 ml) and the combined organic solutions dried and evaporated. The resulting crude product was purified by column chromatography. In examples of crude compounds from the Mitsunobu reaction, the yields for the deprotection step and the quantity of trifluoroacetic acid used were based on the starting homoallylic alcohol.

4-(Phenylsulfonylamino)pent-1-ene 24a.[52] Boc-Sulfonamide **23a** (0.50 g, 1.54 mmol) was deprotected as described in the general procedure to give the crude product as a yellow oil, which was purified by cc (hexane–ethyl acetate 60 : 40) to afford the *title compound* **24a** (0.28 g, 82%) as a viscous, colourless oil: R_f 0.67 (hexane–ethyl acetate 60 : 40); δ_H (250) 7.92–7.49 (5H, m, Ph), 5.57 (1H, ddt, *J* 15.6, 12.4 and 6.4, 2-H), 5.02–4.87 (2H, m, 1-CH_2), 3.49 (1H, qdd, *J* 8.4, 6.3 and 6.2, 4-H), 2.20–2.03 (2H, m, 3-CH_2) and 1.07 (3H, d, *J* 8.4, 5-Me); δ_C (67.8) 140.9 (Ar-C), 133.3 (Ar-CH), 132.4 (2-CH), 128.9, 126.9 (both Ar-CH), 118.5 (1-CH_2), 49.3 (4-CH), 41.3 (3-CH_2) and 21.0 (5-Me); *m*/*z* (EI) 210 ($M^+ - 15$, 1%), 184 (93), 141 (72), 125 (3), 86 (8), 77 (100) and 59 (7).

(*E*)-1-(*p*-Tolylsulfonylamino)hex-3-ene 24b. (*E*)-Hex-3-en-1-ol (0.50 g, 5.0 mmol) was reacted with Mitsunobu reagent **17b** (1.35 g, 5 mmol) under the conditions described above to give the (*E*)-Boc-sulfonamide **23b** as a yellow semi-solid which was not further purified but which was immediately deprotected.

Crude (*E*)-Boc-sulfonamide **23b** from the Mitsunobu reaction was treated with trifluoroacetic acid (5.7 ml, 50 mmol) as described above and the crude product purified by cc (hexane–

ethyl acetate 60 : 40) to yield the *sulfonamide* **24b** (0.86 g, 67%) as a colourless, viscous oil: R_f 0.70 (hexane–ethyl acetate 60 : 40); ν_{max}/cm^{-1} 3272 (NH), 2968 (s), 2923 (s), 1598 (w) and 1315 (s); δ_H (250) 7.73 (2H, d, *J* 8.3, Ar-H), 7.30 (2H, d, *J* 8.3, Ar-H), 5.45 (1H, dt, *J* 15.5 and 6.2, 4-H), 5.16 (1H, dt, *J* 15.5 and 7.1, 3-H), 4.62 (1H, m, NH), 2.99–2.91 (2H, m, 1-CH_2), 2.42 (3H, s, Ar-Me), 2.15–2.08 (2H, m, 2-CH_2), 1.93 (2H, qd, *J* 7.4 and 6.2, 5-CH_2) and 0.90 (3H, t, *J* 7.4, 6-Me); δ_C (67.8) 143.3, 139.9 (both Ar-C), 135.9 (=CH), 129.6, 127.1 (both Ar-CH), 124.3 (=CH), 42.6 (1-CH_2), 32.3, 25.4 (both CH_2), 21.5 (Ar-Me) and 13.6 (6-Me); *m*/*z* (ES) 254 (M^+ + 1, 100%), 252 (22), 224 (13), 184 (6) and 83 (4) [Found: M^+ + 1, 254.1214. $C_{13}H_{20}NO_2S$ requires *M*, 254.1215].

(*E*)-1-(Phenylsulfonylamino)hex-3-ene 24c. (*E*)-Hex-3-en-1-ol (0.21 g, 2.0 mmol) was reacted with Mitsunobu reagent **17a** (0.54 g, 5 mmol) under the conditions described above to give the (*E*)-Boc-sulfonamide **23c** as a yellow semi-solid which was not further purified but which was immediately deprotected.

Crude (*E*)-Boc-sulfonamide **23c** was treated with trifluoroacetic acid (2.3 ml, 20 mmol) as described above and the crude product purified by cc (hexane–ethyl acetate 60 : 40) to afford the *title compound* **24c** (0.35g, 70%) as a colourless, viscous oil: R_f 0.70 (hexane–ethyl acetate 60 : 40); ν_{max}/cm^{-1} 3275 (NH), 2970 (s), 2925 (s), 1660 (w), and 1317 (s); δ_H (250) 7.91–7.46 (5H, m, Ph), 5.44 (1H, dt, *J* 15.5 and 6.2, 4-H), 5.22 (1H, dt, *J* 15.5 and 7.1, 3-CH), 3.02–2.91 (2H, m, 1-CH_2), 2.20–2.08 (2H, m, 2-CH_2), 1.93 (2H, qd, *J* 7.4 and 6.2, 5-CH_2) and 0.90 (3H, t, *J* 7.4, 6-Me); δ_C (67.8) 139.8 (Ar-C), 135.4 (Ar-CH), 132.3 (=CH), 129.2, 126.8 (both Ar-CH), 124.1 (=CH), 42.6 (1-CH_2), 32.2, 25.2 (both CH_2) and 13.3 (6-Me); *m*/*z* (EI) 240 (M^+ + 1, 5%), 198 (6), 170 (90), 141 (97), 125 (6), 82 (7), 77 (100), 69 (14), 51 (47) and 41 (44) [Found: M^+ + 1, 240.1048. $C_{12}H_{18}NO_2S$ requires *M*, 240.1058].

(*E*)-2-(*p*-Tolylsulfonylamino)non-4-ene 24d. Racemic (*E*)-non-4-en-2-ol (0.60 g, 4.2 mmol) was reacted with Mitsunobu reagent **17b** (1.14 g, 4.2 mmol) under the conditions described above to give the *sulfonamide* **23d** (1.20 g, 74%) as a pale yellow, viscous oil: R_f 0.67 (dichloromethane); ν_{max}/cm^{-1} 3010 (w), 2980 (s), 2963 (s), 2880 (s), 1735 (C=O), 1384 (s) and 1295 (s); δ_H (250) 7.80 (2H, d, *J* 8.3, Ar-H), 7.29 (2H, d, *J* 8.3, Ar-H), 5.46 (1H, dt, *J* 15.2 and 6.5, 5-H), 5.29 (1H, dt, *J* 15.2 and 6.6, 4-H), 4.56 (1H, qt, *J* 6.8 and 6.6, 2-H), 2.68–2.33 (2H, m, 3-CH_2), 2.43 (3H, s, Ar-Me), 1.46 (3H, d, *J* 6.8, 1-Me), 1.37 (9H, s, ^{t}Bu), 1.33–1.26 (4H, m, 7- and 8-CH_2) and 0.88 (3H, t, *J* 8.6, 9-Me); δ_C (67.8) 150.6 (C=O), 143.6, 136.9 (both Ar-C), 133.7 (=CH), 128.9, 127.8 (both Ar-CH), 126.4 (=CH), 83.8 (^{t}Bu-C), 55.5 (2-CH), 37.9, 32.2, 31.4 (all CH_2), 27.87 (^{t}Bu-Me), 22.2 (CH_2), 21.5 (Ar-Me), 19.8 (1-Me) and 14.0 (9-Me).

(*E*)-Boc-Sulfonamide **23d** (1.98 g, 5.0 mmol) was deprotected as described in the general procedure and the product purified by cc (dichloromethane) to yield the *title compound* **24d** (1.15 g, 78%) as a pale yellow, viscous oil: R_f 0.36 (dichloromethane); ν_{max}/cm^{-1} 3274 (NH), 2963 (s), 2935 (s), 2864 (w), 1603 (w) and 1459 (s); δ_H (250) 7.75 (2H, d, *J* 8.3, Ar-H), 7.30 (2H, d, *J* 8.3, Ar-H), 5.38 (1H, dt, *J* 15.2 and 6.6, 5-H), 5.10 (1H, dt, *J* 15.2 and 7.2, 4-H), 4.33 (1H, d, *J* 7.2, NH), 3.31 (1H, dqt, *J* 7.2, 6.5 and 6.2, 2-H), 2.43 (3H, s, Ar-Me), 2.04 (2H, dd, *J* 7.2 and 6.2, 3-CH_2), 1.94–1.91 (2H, m, 6-CH_2), 1.38–1.13 (4H, m, 7- and 8-CH_2), 1.09 (3H, d, *J* 6.5, 1-Me) and 0.90 (3H, t, *J* 7.0, 9-Me); δ_C (100) 143.6, 138.3 (Ar-C), 135.5 (=CH), 130.0, 127.5 (both Ar-CH), 124.9 (=CH), 49.9 (2-CH), 40.5, 32.6, 31.8, 22.6 (all CH_2), 21.7 (Ar-Me), 19.0 (1-Me) and 14.3 (9-Me); *m*/*z* (FAB) 296 (M^+ + 1, 23%), 289 (15), 254 (6), 198 (18), 154 (100), 137 (70), 120 (12), 107 (21), 95 (6) and 77 (17) [Found: C, 63.5; H, 8.6; N, 4.5; M^+ + 1, 296.1693. $C_{16}H_{25}NO_2S$ requires C, 64.0; H, 8.5; N, 4.7%; $C_{16}H_{26}NO_2S$ requires *M*, 296.1684].

(2*R*)-(*E*)-2-(*p*-Tolylsulfonylamino)non-4-ene 24e. (2*R*)-(*E*)-Non-4-en-2-ol (0.34 g, 2.40 mmol) was reacted with Mitsunobu reagent **17b** (0.65 g, 2.40 mmol) under the conditions described above to give (2*R*)-(*E*)-2-(*N*-*tert*-butoxycarbonyl-*p*-tolylsulfonylamino)non-4-ene **23e** as a yellow, semi-solid which was not further purified but was immediately deprotected.

Crude (*R*)-(*E*)-Boc-sulfonamide **23e** was deprotected with trifluoroacetic acid (2.9 ml, 24 mmol) as described in the general procedure to afford the *title compound* **24e** (0.50 g, 71%) as a pale yellow, viscous oil: $[\alpha]_D$ = +33.5 (*c* 0.01, $CHCl_3$); other spectral data were identical to those displayed by the racemic sulfonamide **24d** (see above).

(*E*)-3-(*p*-Tolylsulfonylamino)dec-5-ene 24f. (*E*)-Boc-Sulfonamide **23f** (0.50 g, 1.2 mmol) was deprotected as described above and purified by cc (dichloromethane) to afford the *sulfonamide* **24f** (0.34 g, 92%) as a viscous, colourless oil: R_f 0.36 (dichloromethane); ν_{max}/cm^{-1} 3280 (NH), 2959 (s), 2927 (s), 2872 (w), 1598 (w), 1454 (s) and 1327 (s); δ_H (400) 7.77 (2H, d, *J* 8.3, Ar-H), 7.28 (2H, d, *J* 8.3, Ar-H), 5.34 (1H, dt, *J* 15.5 and 6.6, 6-H), 5.10 (1H, dt, *J* 15.5 and 7.3, 5-H), 4.91 (1H, d, *J* 7.9, NH), 3.14 (1H, dtt, *J* 7.9, 7.3 and 6.5, 3-H), 2.41 (3H, s, Ar-Me), 2.03 (2H, app. dd, *J* 7.3 and 6.5, 4-CH_2), 1.96–1.82 (2H, m, 7-CH_2), 1.44 (2H, dq, *J* 7.3 and 6.9, 2-CH_2), 1.28–1.23 (4H, m, 8- and 9-CH_2), 0.87 (3H, t, *J* 6.9, 1-Me) and 0.81 (3H, t, *J* 7.4, 10-Me); δ_C (100) 142.8, 138.3 (both Ar-C), 134.6 (=CH), 129.3, 126.9 (both Ar-CH), 124.4 (=CH), 54.9 (3-CH), 37.1, 32.1, 31.3, 27.3, 22.0 (all CH_2), 21.3 (Ar-Me), 13.7 (10-Me) and 9.6 (1-Me), *m*/*z* (ES) 310 (M^+ + 1, 100), 279 (6), 139 (13) and 83 (12) [Found: M^+ + 1, 310.1843. $C_{17}H_{28}NO_2S$ requires *M*, 310.1841].

(*E*)-3-(Methylsulfonylamino)dec-5-ene 24g. (*E*)-Boc-Sulfonamide **23g** (0.20 g, 0.65 mmol) was deprotected as described above and purified by cc (dichloromethane) to yield the *title compound* **24g** (0.12 g, 77%) as a pale yellow, viscous oil: R_f 0.39 (dichloromethane); ν_{max}/cm^{-1} 3286 (NH), 2960 (s), 2930 (s), 2874 (w), 1581 (w), 1434 (s), 1413 (s) and 1379 (s); δ_H (270) 5.39 (1H, dt, *J* 15.2 and 6.6, 6-H), 5.22 (1H, dt, *J* 15.2 and 7.2, 5-H), 4.22 (1H, d, *J* 8.3, NH), 3.15 (1H, dtt, *J* 8.3, 8.0 and 6.9, 3-H), 2.79 (3H, s, SO_2Me), 2.08 (2H, dd, *J* 7.2 and 6.9, 4-CH_2), 1.87 (2H, m, 7-CH_2), 1.52 (2H, dq, *J* 8.0 and 7.1, 2-CH_2), 1.24–1.03 (4H, m, 8- and 9-CH_2), 0.80 (3H, t, *J* 7.2, 10-Me) and 0.74 (3H, t, *J* 7.1, 1-Me); δ_C (67.8) 135.3, 124.5 (both =CH), 55.5 (3-CH), 41.8 (SO_2Me), 38.0, 32.2, 31.4, 27.9, 22.2 (all CH_2), 13.8 (10-Me) and 10.0 (1-Me); *m*/*z* (ES) 234 (M^+ + 1, 100%), 231 (33), 172 (70) and 62 (35) [Found: M^+ + 1, 234.1530. $C_{11}H_{24}NO_2S$ requires *M*, 234.1528].

(*E*)-3-(*p*-Tolylsulfonylamino)undec-5-ene 24h. (*E*)-Undec-5-en-3-ol (1.00 g, 6.3 mmol) was reacted with Mitsunobu reagent **17b** (1.71 g, 6.3 mmol) under the conditions described in the general procedure to give the Boc-sulfonamide **23h** as an orange semi-solid which was not further purified but was immediately deprotected.

Crude (*E*)-Boc-sulfonamide **23h** was treated with trifluoroacetic acid (7.2 ml, 62 mmol) as described above and the crude product purified by cc (dichloromethane) to afford the *sulfonamide* **24h** (0.14 g, 68%) as a viscous, colourless oil: R_f 0.37 (dichloromethane); ν_{max}/cm^{-1} 3280 (NH), 2958 (s), 2927 (s), 2870 (w), 1600 (w), 1453 (s) and 1328 (s); δ_H (400) 7.77 (2H, d, *J* 8.2, Ar-H), 7.28 (2H, d, *J* 8.2, Ar-H), 5.37 (1H, dt, *J* 15.4 and 6.6, 6-H), 5.09 (1H, dt, *J* 15.4 and 7.4, 5-H), 4.55 (1H, d, *J* 7.9, NH), 3.14 (1H, dtt, *J* 7.9, 7.4 and 6.6, 3-H), 2.42 (3H, s, Ar-Me), 2.03 (2H, dd, *J* 7.4 and 6.6, 4-CH_2), 1.91–1.77 (2H, m, 7-CH_2), 1.43 (2H, dq, *J* 7.4 and 6.9, 2-CH_2), 1.39–1.17 (6H, m, 8-, 9- and 10-CH_2), 0.87 (3H, t, *J* 6.9, 1-Me) and 0.82 (3H, t, *J* 7.4, 10-Me); δ_C (100) 143.0, 138.2 (both Ar-C), 135.0 (=CH), 129.5, 126.9 (both Ar-CH), 124.3 (=CH), 54.9 (3-CH), 37.1,

32.5, 31.4, 29.1, 27.4, 22.4 (all CH_2), 21.3 (Ar-Me), 14.0 (10-Me) and 9.8 (1-Me) [Found: (APcI) $M^+ + 1$, 324.1994. $C_{18}H_{30}NO_2S$ requires *M*, 324.1997].

(*E*)-5-(*p*-Tolylsulfonylamino)tridec-7-ene 24i. (*E*)-Boc-Sulfonamide **23i** (2.20 g, 4.8 mmol) was deprotected as described in the general procedure and the product purified by cc (hexane–ethyl acetate 9 : 1) to afford the *title compound* **24i** (1.30 g, 77%) as a colourless, viscous oil: R_f 0.43 (hexane–ethyl acetate 9 : 1); ν_{max}/cm^{-1} 3278 (NH), 2955 (w), 2929 (s), 2858 (s), 1778 (w), 1598 (w), 1457 (s), 1425 (s) and 1326 (s); δ_H (250) 7.77 (2H, d, *J* 8.3, Ar-H), 7.28 (2H, d, *J* 8.3, Ar-H), 5.30 (1H, dt, *J* 15.1 and 6.6, 8-H), 5.05 (1H, dt, *J* 15.1 and 7.2, 7-H), 4.72 (1H, d, *J* 7.9, NH), 3.21 (1H, m, 5-H), 2.47 (3H, s, Ar-Me), 2.15–1.72 (6H, m, 4-, 6- and 9-CH_2), 1.52–1.03 (10H, m, 2-, 3-, 10-, 11- and 12-CH_2), 0.97 (3H, t, *J* 7.2, 1-Me) and 0.86 (3H, t, *J* 7.1, 13-Me); δ_C (100) 143.1, 138.4 (both Ar-C), 135.3 (=CH), 129.5, 127.1 (both Ar-CH), 124.3 (=CH), 54.1 (5-CH), 34.9, 34.8, 31.5, 31.4, 27.5, 27.4, 24.9, 22.6 (all CH_2), 22.5 (Ar-Me) and 13.9 (1- and 13-Me); *m*/*z* (ES) 352 ($M^+ + 1$, 100%), 350 (46), 312 (42), 172 (78) and 60 (39) [Found: $M^+ + 1$, 352.2310. $C_{20}H_{34}NO_2S$ requires *M*, 352.2310].

(*E*)-4-(*p*-Tolylsulfonylamino)-1-phenylhex-1-ene 24j. (*E*)-Boc-Sulfonamide **23j** (3.00 g, 7 mmol) was deprotected as described above using trifluoroacetic acid (7.98 g, 70 mmol) and the product purified by cc (hexane–ethyl acetate 9 : 1) to yield the *title compound* **24j** (2.20 g, 95%) as a colourless, crystalline solid, mp 76–77 °C: R_f 0.26 (dichloromethane); ν_{max}/cm^{-1} ($CHCl_3$) 3280 (NH), 2965 (s), 2931 (s), 2875 (w), 1597 (w), 1448 (s), 1422 (s) and 1324 (s); δ_H (250) 7.74 (2H, d, *J* 8.2, Ar-H), 7.31–7.19 (7H, m, Ar-H), 6.28 (1H, d, *J* 15.8, 1-H), 5.86 (1H, dt, *J* 15.8 and 7.4, 2-H), 4.69 (1H, d. *J* 7.2, NH), 3.28 (1H, dtt, *J* 7.2, 7.0 and 6.7, 4-H), 2.38 (3H, s, Ar-Me), 2.27 (2H, dd, *J* 7.4 and 6.7, 3-CH_2), 1.54 (2H, qd, *J* 7.6 and 7.0, 5-CH_2) and 0.85 (3H, t, *J* 7.6, 6-Me); δ_C (100) 141.6, 136.4, 135.1 (all Ar-C), 131.9 (=CH), 128.0, 126.9, 125.8, 125.5, 124.5, (all Ar-CH), 123.5 (=CH), 53.6 (4-CH), 36.3, 26.3 (both CH_2), 19.9 (Ar-Me) and 8.3 (6-Me); *m*/*z* (ES) 330 ($M^+ + 1$, 100%), 176 (7) and 159 (19) [Found: C, 69.3; H, 7.3; N, 4.45. $C_{19}H_{23}NO_2S$ requires C, 69.3; H, 7.0; N, 4.25%].

(*E*)-4-Phenylsulfonylamino-1-phenylhex-1-ene 24k. (*E*)-1-Phenylhex-1-en-4-ol (2.47 g, 14 mmol) was reacted with the Mitsunobu reagent **17a** (3.59 g, 14 mmol) under the conditions described in the general procedure to give a crude product **23k** which was deprotected immediately by treatment with trifluoroacetic acid (16 g, 140 mmol) as described above. Purification of the residue by cc (hexane–ethyl acetate 9 : 1) gave the *benzenesulfonamide* **24k** (3.175 g, 72%) as a colourless, crystalline solid, mp 82–83 °C: R_f 0.24 (dichloromethane); ν_{max}/cm^{-1} ($CHCl_3$) 3270 (NH), 2980 (s), 2930 (s), 2875 (w), 1600 (w), 1450 (s), 1410 (s) and 1320 (s); δ_H 7.85–7.14 (10H, m, 2 × Ph), 6.24 (1H, d, *J* 15.6, 1-H), 5.79 (1H, dt, *J* 15.6 and 7.3, 2-H), 4.87 (1H, d, *J* 7.1, NH), 3.23 (1H, dtt, *J* 7.1, 6.9 and 6.7, 4-H), 2.33 (2H, dd, *J* 7.3 and 6.7, 3-CH_2), 1.55 (2H, qd, *J* 7.6 and 6.9, 5-CH_2) and 0.87 (3H, t, *J* 7.6, 6-Me); *m*/*z* (ES) 316 ($M^+ + 1$, 100%) [Found: C, 68.5; H, 6.9; N, 4.5. $C_{18}H_{21}NO_2S$ requires C, 68.5; H, 6.7; N, 4.4%].

(*Z*)-1-(*p*-Tolylsulfonylamino)hex-3-ene 26a. (*Z*)-Boc-Sulfonamide **25a** (1.30 g, 3.7 mmol) was deprotected as described above and the crude product purified by cc (dichloromethane) to give the *sulfonamide* **26a** (0.70 g, 72%) as a viscous, colourless oil: R_f 0.43 (dichloromethane); ν_{max}/cm^{-1} 3284 (NH), 2964 (s), 2934 (s), 1656 (w), 1598 (w), 1426 (s) and 1325 (s); δ_H (400) 7.76 (2H, d, *J* 8.2, Ar-H), 7.30 (2H, d, *J* 8.2, Ar-H), 5.49 (1H, dt *J* 10.8 and 7.3, 4-H), 5.25 (1H, dt *J* 10.8 and 7.3, 3-H), 5.01 (1H, t, *J* 6.1, NH), 2.95 (2H, td, *J* 6.9 and 6.1, 1-CH_2), 2.42 (3H, s, Ar-Me), 2.20 (2H, dt, *J* 7.3 and 6.9, 2-CH_2), 2.01 (2H, qd, *J* 7.6 and 7.3, 5-CH_2) and 0.92 (3H, t, *J* 7.6, 6-Me); δ_C (100) 143.2, 136.5 (both Ar-C), 135.0 (=CH), 129.5, 127.0 (both Ar-CH), 123.1 (=CH), 42.7 (1-CH_2), 27.2, 21.3 (both CH_2), 20.4 (Ar-Me) and 14.0 (6-Me); *m*/*z* (FAB) 254 ($M^+ + 1$, 100%), 184 (33), 154 (61), 137 (53), 107 (18), 91 (23) and 77 (15) [Found: $M^+ + 1$, 254.1240. $C_{13}H_{20}NO_2S$ requires *M*, 254.1215].

(*Z*)-1-(Methylsulfonylamino)hex-3-ene 26b. (*Z*)-Boc-Sulfonamide **25b** (0.21 g, 0.80 mmol) was deprotected as described above and purified by cc (dichloromethane) to yield the *title compound* **26b** (0.16 g, 71%) as a colourless, viscous oil: R_f 0.38 (dichloromethane); ν_{max}/cm^{-1} 3287 (NH), 2964 (s), 2875 (s), 1655 (w), 1437 (s) and 1317 (s); δ_H (400) 5.49 (1H, dt, *J* 10.7 and 7.3, 4-H), 5.24 (1H, dt, *J* 10.7 and 7.3, 3-H), 4.92–4.79 (1H, br, s, NH), 3.08 (2H, td, *J* 6.9 and 6.4, 1-CH_2), 2.91 (3H, s, SO_2Me), 2.27 (2H, dt, *J* 7.3 and 6.9, 2-CH_2), 2.01 (2H, qd, *J* 7.5 and 7.3, 5-CH_2) and 0.93 (3H, t, *J* 7.5, 6-Me); δ_C (100) 135.0, 124.0 (both =CH), 42.8 (1-CH_2), 39.9 (SO_2Me), 27.7, 20.5 (both CH_2) and 14.0 (Me); *m*/*z* (FAB) 178 ($M^+ + 1$, 43%), 154 (100), 137 (81), 108 (27), 89 (20), 77 (22) and 55 (18).

(*Z*)-3-(Tolylsulfonylamino)dec-5-ene 26c. (*Z*)-Dec-5-en-3-ol (0.40 g, 0.26 mmol) was reacted with Mitsunobu reagent **17b** (0.69 g, 0.26 mmol) under the conditions described above to afford *N*-Boc-sulfonamide **25c** as a yellow, semi-solid which was not further purified but which was immediately deprotected.

Crude (*Z*)-Boc-sulfonamide **25c** was treated with trifluoroacetic acid (2.9 ml, 26.0 mmol) as described above and the crude product purified by cc (dichloromethane) to afford the *title compound* **26c** (0.05 g, 74%) as a viscous, colourless oil: R_f 0.38 (dichloromethane); ν_{max}/cm^{-1} 3274 (NH), 2964 (s), 2938 (s), 2862 (w), 1601 (w) and 1500 (s); δ_H (270) 7.83 (2H, d, *J* 7.9, Ar-H), 7.33 (2H, d, *J* 7.9, Ar-H), 5.47–5.19 (3H, m, NH, 5- and 6-H), 3.25–3.17 (1H, m, 3-H), 2.45 (3H, s, Ar-Me), 2.21–2.16 (2H, m, 4-CH_2), 2.07–1.97 (2H, m, 7-CH_2), 1.59–1.29 (6H, m, 2-, 8- and 9-CH_2), 0.91 (3H, t, *J* 6.9, 1-Me) and 0.84 (3H, t, *J* 7.4, 10-Me); δ_C (67.8) 143.2, 138.6 (both Ar-C), 133.4 (=CH), 129.7, 127.3 (both Ar-CH), 124.3 (=CH), 55.6 (3-CH), 32.4, 31.9, 27.4, 27.2, 22.5 (all CH_2), 21.7 (Ar-Me), 14.2 (10-Me) and 9.9 (1-Me); *m*/*z* (FAB) 310 ($M^+ + 1$, 53%), 212 (100), 155 (41), 137 (19), 91 (36), 83 (20) and 54 (16) [Found: $M^+ + 1$, 310.1846. $C_{17}H_{28}NO_2S$ requires *M*, 310.1840].

(2*RS*,3*RS*)-(*E*)-2-(*p*-Tolylsulfonylamino)-3-methyloct-4-ene 27b. (2*SR*,3*RS*)-(*E*)-3-Methyloct-4-en-2-ol [(*E*)-*syn*-alkenol] (0.80 g, 5.62 mmol), derived from *cis*-2,3-epoxybutane, was reacted with Mitsunobu reagent **17b** (1.53 g, 5.62 mmol) under the conditions described in the general procedure to afford the (*E*)-*anti*-Boc-sulfonamide **27a** as an orange semi-solid which was not further purified but which was immediately deprotected.

A solution of crude (*E*)-*anti*-Boc-sulfonamide **27a** in dichloromethane (50 ml) was deprotected as described above using trifluoroacetic acid (5.7 g, 56 mmol). The product was purified by cc (dichloromethane) to afford the *sulfonamide* **27b** (1.32 g, 80%) as a colourless, viscous oil: R_f 0.48 (dichloromethane); ν_{max}/cm^{-1} 3282 (NH), 2973 (s), 2931 (s), 2875 (w), 1581 (w), 1454 (s), 1328 (s) and 1166 (s); δ_H (250) 7.74 (2H, d, *J* 8.3, Ar-H), 7.29 (2H, d, *J* 8.3, Ar-H), 5.37 (1H, dt, *J* 15.2 and 6.6, 5-H), 5.12 (1H, ddd, *J* 15.2, 8.3 and 1.2, 4-H), 4.34 (1H, d, *J* 8.7, NH), 3.29–3.20 (1H, m, 2-H), 2.43 (3H, s, Ar-Me), 2.16–2.07 (1H, m, 3-CH), 1.93 (2H, td, *J* 7.1 and 6.6, 6-CH_2), 1.35 (2H, qt, *J* 7.4 and 7.1, 7-CH_2), 0.97 (3H, d, *J* 6.7, 1-Me), 0.90 (3H, d, *J* 6.8, 3-Me) and 0.86 (3H, t, *J* 7.4, 8-Me); δ_C (67.8) 143.6, 139.8 (both Ar-C), 133.1 (Ar-CH), 130.1, 129.6 (both =CH), 127.6 (Ar-CH), 53.6 (2-CH), 42.2 (3-CH), 34.6, 22.5 (both CH_2), 21.5 (Ar-Me), 17.4 (1-Me), 17.1 (3-Me) and 13.6 (8-Me); *m*/*z* (FAB) 296 ($M^+ + 1$, 93%), 198 (100), 155 (48), 125 (84), 107 (12), 91 (47), 83 (41) and 69 (78) [Found: C, 64.6; H, 8.6; N, 4.55;

$M^+ + 1$, 296.1734. $C_{16}H_{25}NO_2S$ requires C, 65.0; H, 8.5; N, 4.7%; $C_{16}H_{26}NO_2S$ requires *M*, 296.1684].

(2*SR*,3*RS*)-(*E*)-2-(*p*-Tolylsulfonylamino)-3-methyloct-4-ene 28b. (2*SR*,3*SR*)-(*E*)-3-Methyloct-4-en-2-ol [(*E*)-*anti*-alkenol] (0.30 g, 2.20 mmol), derived from *trans*-2,3-epoxybutane, was reacted with Mitsunobu reagent **17b** (0.57 g, 2.20 mmol) under the conditions described in the general procedure to give the (*E*)-*syn*-Boc-sulfonamide **28a** as an orange semi-solid which was not further purified but which was immediately deprotected.

A solution of crude (*E*)-*syn*-Boc-sulfonamide **28a** in dichloromethane (20 ml) was deprotected using trifluoroacetic acid (2.4 ml, 21 mmol) as described above and the product purified by cc (dichloromethane) to give the *title compound* **28b** (0.53 g, 86% yield) as a colourless, viscous oil: R_f 0.49 (dichloromethane); ν_{max}/cm^{-1} 3282 (NH), 2973 (s), 2931 (s), 2882 (s), 1588 (w), 1440 (s) and 1328 (s); δ_H (400) 7.76 (2H, d, *J* 8.3, Ar-H), 7.29 (2H, d, *J* 8.3, Ar-H), 5.40 (1H, dt, *J* 15.3 and 6.8, 5-H), 5.74 (1H, ddd, *J* 15.3, 7.9 and 1.2, 4-H), 4.76 (1H, d, *J* 7.3, NH), 3.14 (1H, m, 2-H), 2.42 (3H, s, Ar-Me), 2.10 (1H, m, 3-H), 1.90 (2H, td, *J* 7.3 and 6.8, 6-CH_2), 1.32 (2H, tq, *J* 7.3 and 7.3, 7-CH_2), 0.99 (3H, d, *J* 6.6, 1-Me), 0.90 (3H, d, *J* 6.8, 3-Me) and 0.86 (3H, t, *J* 7.3, 8-Me); δ_C (100) 143.0, 138.0 (both Ar-C), 132.4 (Ar-CH), 130.8, 129.4 (both =CH), 127.0 (Ar-CH), 53.9 (2-CH), 42.1 (3-CH), 34.5, 22.4 (both CH_2), 21.4 (Ar-Me), 18.8 (1-Me), 16.2 (3-Me) and 13.5 (8-Me); *m*/*z* (FAB) 296 ($M^+ + 1$, 46%), 198 (50), 154 (57), 137 (48), 125 (43), 107 (27), 91 (72), 83 (32) and 69 (100) [Found: $M^+ + 1$, 296.1697. $C_{16}H_{26}NO_2S$ requires *M*, 296.1684].

(1*RS*,2*RS*)-2-(Hex-1-ynyl)-1-(*p*-tolylsulfonylamino)cyclohexane 30b. To a stirred solution of phthalimide **30a** (1.0 g, 3.5 mmol) in ethanol (4 ml) was added hydrazine monohydrate (3.85 ml). The resulting solution was heated at reflux for 2 h, then cooled and acidified with concentrated hydrochloric acid. The phthalhydrazide was removed by filtration and the solid washed with ethanol (4 × 10 ml). The filtrate was diluted with water (50 ml), and the solution reduced to 20 ml under reduced pressure and filtered. The solvent was then completely removed and the remaining amine salt dissolved in dichloromethane (10 ml). The resulting solution was treated with *toluene-p*-sulfonyl chloride (0.74 g, 3.85 mmol) and triethylamine (1.1 ml, 7.7 mmol) and stirred at ambient temperature for 16 h then washed successively with 2 M hydrochloric acid (2 × 5 ml), saturated aqueous sodium hydrogencarbonate (5 ml) and brine (10 ml). The remaining organic solution was dried and evaporated and the crude product purified by cc (hexane–ether 80 : 20) to afford the *toluene-p-sulfonamide* **30b** (0.55 g, 47%) as a pale yellow oil: ν_{max}/cm^{-1} 3372 (NH), 1738 (w), 1599 (w), 1415 (s) and 1331 (s); δ_H (400) 7.77 (2H, d, *J* 8.2, Ar-H), 7.27 (2H, d, *J* 8.2, Ar-H), 4.89 (1H, d, *J* 8.2, NH), 3.20–3.17 (1H, m, 1-H), 2.60 (1H, app br s, 2-H), 2.41 (3H, s, Ar-Me), 2.15 (2H, td, *J* 6.9 and 2.2, 3′-CH_2), 1.80–1.25 (12H, m) and 0.91 (3H, t, *J* 7.1, Me); δ_C (100) 143.0, 138.5 (both Ar-C), 129.5, 126.7 (both Ar-CH), 84.9, 77.8 (both C), 55.6, 33.7 (both CH), 31.0, 30.4, 29.7, 24.6, 21.9 (all CH_2), 21.4 (Ar-Me), 20.6, 18.2 (both CH_2) and 13.6 (Me); *m*/*z* (ES) 334 ($M^+ + 1$, 100%), 189 (42) and 124 (19) [Found: $M^+ + 1$, 334.1841. $C_{19}H_{28}NO_2S$ requires *M*, 334.1843].

(*E*)-(1*RS*,2*RS*)-2-(Hex-1-en-1-yl)-1-(*p*-tolylsulfonylamino)-cyclohexane 31. To a stirred solution of sulfonamide **30b** (0.10 g, 0.30 mmol) in THF (10 ml) was added lithium aluminium hydride (1 M solution in THF, 3.0 ml, 3.0 mmol) and the resulting solution refluxed for 48 h. The solution was then cooled and excess reagent was quenched by the dropwise addition of water. The resulting white solid was removed by filtration. The filtrate was evaporated, and the residue dissolved in dichloromethane (10 ml) and treated with triethylamine (50 μl, 0.30 mmol) and *toluene-p*-sulfonyl chloride (78 mg, 0.30 mmol). The resulting solution was stirred at ambient temperature for 2 days then diluted with dichloromethane and washed successively with 2 M hydrochloric acid (3 × 2 ml), saturated aqueous sodium hydrogencarbonate (3 ml) and brine (3 ml). The organic solution was then dried and evaporated and the residue purified by cc (hexane–ether 80 : 20) to furnish the (*E*)-*toluene-p-sulfonamide* **31** (40 mg, 41%) as a viscous oil: ν_{max}/cm^{-1} 1600 (s), 1415 (s) and 1178 (s); δ_H (400) 7.73 (2H, d, *J* 8.0, Ar-H), 7.29 (2H, d, *J* 8.0, Ar-H), 5.32 (1H, dt, *J* 15.5 and 6.5, 2′-H), 5.23 (1H, dd, *J* 15.5 and 7.5, 1′-H), 4.40 (1H, d, *J* 7.3, NH), 3.30–3.26 (1H, m, 1-H), 2.43 (3H, s, Ar-Me), 2.20–2.13 (1H, m, 2-H), 1.95–1.90 (2H, m, 3′-CH_2), 1.63-1.20 (12H, m) and 0.91 (3H, t, *J* 7.0, Me); δ_C (100) 142.7, 137.9 (both Ar-C), 133.6 (=CH), 129.3, 128.1 (both Ar-CH), 126.8 (=CH), 53.5, 42.2 (both CH), 32.2, 31.3, 30.2, 28.4, 22.6 (all CH_2), 22.0 (Ar-Me), 21.1 (CH_2) and 13.7 (Me).

(*Z*)-(1*RS*,2*RS*)-2-(Hex-1-en-1-yl)-1-(*p*-tolylsulfonylamino)-cyclohexane 32. The tosylated acetylene **30b** (54 mg, 0.16 mmol) was dissolved in ethyl acetate (1 ml) and 5% palladium on barium sulfate (7 mg, 0.016 mmol) was added. The resulting suspension was stirred under an atmosphere of hydrogen for 3 h. The catalyst was removed by filtration and the solvent evaporated to give a crude product which was purified by cc (hexane–ether 80 : 20) to afford the (*Z*)-*toluene-p-sulfonamide* **32** (50 mg, 95%) as a pale yellow oil: ν_{max}/cm^{-1} 1721 (m), 1600 (s), 1415 (s) and 1178 (s); δ_H (400) 7.74 (2H, d, *J* 8.2, Ar-H), 7.28 (2H, d, *J* 8.2, Ar-H), 5.48–5.38 (2H, m, 1′- and 2′-H), 4.49 (1H, d, *J* 6.6, NH), 3.35–3.30 (1H, br s, 1-H), 2.61–2.58 (1H, m, 2-H), 2.43 (3H, s, Ar-Me), 1.88–1.85 (2H, m, 3′-CH), 1.62–1.11 (12H, m) and 0.88 (3H, t, *J* 7.0, Me); δ_C (100) 142.9, 137.9 (both Ar-C), 133.8 (=CH), 129.5, 126.9 (both Ar-CH), 126.7 (=CH), 54.2, 37.1 (both CH), 31.8, 30.3, 30.0, 27.2, 23.8, 22.3 (all CH_2), 21.5 (Ar-Me), 21.1 (CH_2) and 13.9 (Me).

2-Methyloct-4-enoic acid 34. To a stirred solution of hex-1-en-3-ol (5.00 g, 50.0 mmol), triethylamine (6.05 ml, 50.0 mmol) and 4-dimethylaminopyridine (10 mg) in dichloromethane at 0 °C was added dropwise propionyl chloride (4.77 ml, 55.0 mmol). The reaction mixture was heated to reflux for 2 h, then cooled and washed with aqueous 2 M hydrochloric acid (2 × 30 ml). The organic solution was dried and evaporated to leave a yellow oil which was purified by cc (dichloromethane) to afford the *propionate* **33** (7.20 g, 85%) as a colourless oil: R_f 0.76 (dichloromethane): ν_{max}/cm^{-1} 2961 (s), 2940 (s), 2876 (w), 1739 (C=O), 1463 (s) and 1362 (s); δ_H (250) 5.76 (1H, ddd, *J* 16.0, 9.4 and 6.2, 2-H), 5.29–5.11 (3H, m, 1-CH_2 and 3-H), 2.32 (2H, q, *J* 7.6, 3′-CH_2), 1.64–1.17 (4H, m, 4-CH_2 and 5-CH_2), 1.14 (3H, t, *J* 7.6, 4-Me) and 0.91 (3H, t, *J* 7.3, 6-Me); δ_C (67.8) 173.7 (C=O), 136.7 (2-CH), 116.7 (1-CH_2), 74.3 (3-CH), 36.3, 27.8, 18.3 (all CH_2), 13.8 (4-Me) and 9.1 (6-Me).

To neat diisopropylamine (2.31 ml, 16.7 mmol), stirred at −78 °C, was added dropwise butyllithium (1.6 M solution in hexanes, 5.10 ml, 11.1 mmol) and the mixture warmed to ambient temperature during 1 h. The hexane was removed by a stream of nitrogen to leave a cream paste which was dissolved in THF (25 ml). The resulting solution of LDA was cooled to −78 °C and unsaturated ester **33** (1.56 g, 10.0 mmol) was added dropwise. The reaction mixture was maintained at −78 °C for 10 minutes, after which trimethylsilyl chloride (1.20 g, 11.1 mmol, freshly distilled from calcium hydride) was added dropwise. The reaction mixture was warmed to ambient temperature during 0.5 h then refluxed for 1 h. The reaction mixture was cooled to ambient temperature, poured into aqueous 2 M sodium hydroxide (30 ml) and the mixture washed with diethyl ether (3 × 20 ml). The aqueous layer was acidified with concentrated hydrochloric acid, then extracted with dichloromethane (3 × 30 ml). The combined dichloromethane extracts were dried and evaporated to give the *acid* **34** (1.03 g, 66%) as a clear oil: R_f 0.47 (dichloromethane); ν_{max}/cm^{-1} 3112 (OH), 2959 (s), 2663 (s), 1706 (C=O), 1463 (s) and 1418 (s); δ_H (270) 5.56–5.33 (2H,

m, 4- and 5-H), 2.59–2.34 (2H, m, 3-CH_2), 2.21–1.87 (3H, m, 2-H and 6-CH_2), 1.46–1.26 (2H, m, 7-CH_2), 1.18 (3H, d, *J* 7.0, 1′-Me) and 0.90 (3H, t, *J* 7.3, 8-Me); δ_C (67.8) 182.8 (C=O), 133.2, 126.5 (both =CH), 67.8 (2-CH), 36.4, 34.6, 22.5 (all CH_2), 16.1 (1-Me) and 13.5 (8-Me).[53]

(*E*)-2-(*tert*-Butoxycarbonylamino)oct-4-ene 35a. A stirred solution of the foregoing acid **34** (2.60 g, 17.0 mmol), diphenylphosphoryl azide (3.59 ml, 17.0 ml, 17.0 mmol) and triethylamine (2.44 ml, 17.0 mmol) in *tert*-butyl alcohol (50 ml) was refluxed for 18 h. The reaction mixture was cooled, and the *tert*-butyl alcohol removed under reduced pressure. The residue was dissolved in benzene (50 ml) and the solution washed successively with water (30 ml), saturated aqueous sodium carbonate (60 ml) and brine (30 ml). The organic solution was then dried and evaporated to leave a clear oil which was purified by cc (dichloromethane) to afford the *N-Boc amine* **35a** (2.79 g, 72%) as a clear oil: R_f 0.44 (dichloromethane); ν_{max}/cm^{-1} 3342 (NH), 2964 (s), 2872 (s), 1693 (C=O), 1523 (s) and 1248 (s); δ_H (250) 5.42 (1H, dt, *J* 15.5 and 6.6, 5-H), 5.37 (1H, dt, *J* 15.5 and 6.6, 4-H), 4.42–4.28 (1H, m, NH), 3.72–3.57 (1H, m, 2-H), 2.10 (1H, dd, *J* 6.6 and 6.0, 3-H), 1.96 (2H, td, *J* 7.2 and 6.6, 6-CH_2), 1.42 (9H, s, ^{t}Bu), 1.36 (2H, qt, *J* 7.4 and 7.2, 7-CH_2), 1.07 (3H, t, *J* 6.6, 1-Me) and 0.86 (3H, t, *J* 7.4, 8-Me); δ_C (67.8) 133.8, 125.7 (both =CH), 47.4 (2-CH), 40.0, 34.7, 22.5 (all CH_2), 20.5 (1′-Me) and 13.6 (8-Me); *m/z* (FAB) 228 (M^+ + 1, 15%), 172 (100), 154 (10), 144 (29), 88 (33), 68 (27) and 56 (46) [Found: M^+ + 1, 228.1959. $C_{13}H_{26}NO_2$ requires *M*, 228.1963].

(*E*)-2-Aminooct-4-ene 35b. To a stirred solution of the *N*-Boc-amine **35a** (0.40 g, 1.80 mmol) in dichloromethane (20 ml) was added trifluoroacetic acid (2.05 g, 18 mmol) and the solution stirred at ambient temperature for 3h, then neutralised with saturated aqueous sodium hydrogencarbonate, followed by extraction with dichloromethane (3 × 30 ml). The combined organic solutions were dried (sodium sulfate) and evaporated to afford the *amine* **35b** (0.19 g, 86%) as a yellow oil: R_f 0.18 (methanol–dichloromethane 1 : 9); ν_{max}/cm^{-1} 3370 (NH), 2945 (s), 2837 (s), 1460 (s) and 1342 (s); δ_H (270) 5.58 (1H, dt, *J* 15.3 and 6.7, =CH), 5.44 (1H, dt, *J* 15.3 and 7.1, =CH), 3.77–3.65 (1H, m, 2-H), 2.08–1.83 (4H, m, 3- and 6-CH_2), 1.38–1.23 (2H, m, 7-CH_2), 1.05 (3H, d, *J* 6.4, 1-Me) and 0.81 (3H, t, *J* 7.3, 8-Me); δ_C (67.8) 138.2, 122.8 (both =CH), 49.9 (2-CH), 38.3, 35.2, 22.7 (all CH_2), 18.9 (1-Me) and 14.2 (8-Me); *m/z* (FAB) 128 (M^+ + 1, 23%), 73 (10), 69 (17) and 43 (100) [Found: M^+ + 1, 128.1565. $C_8H_{18}N$ requires *M*, 128.1557].

(*E*)-2-Trifluoroacetylaminooct-4-ene 35c. A solution of amine **35b** (0.28 g, 2.20 mmol), trifluoroacetic anhydride (0.24 ml, 2.20 mmol) and triethylamine (0.34 ml, 2.20 mmol) in dichloromethane (20 ml) was stirred at ambient temperature for 2 h. The reaction mixture was then neutralised with 2 M hydrochloric acid and extracted with dichloromethane (3 × 20 ml). The combined organic solutions were dried and evaporated to give a mixture of mono- and diacylated products which were separated by cc (dichloromethane) to afford the *title compound* **35c** (0.31 g, 63%) as a pale yellow oil: R_f 0.37 (dichloromethane); ν_{max}/cm^{-1} 3621 (NH), 3021 (s), 2975 (s), 1723 (C=O), 1527 (s) and 1383 (s); δ_H (270) 5.49 (1H, dt, *J* 15.3 and 6.8, 5-H), 5.35 (1H, dt, *J* 15.3 and 7.1, 4-H), 4.12–4.01 (1H, m, 2-H), 2.21 (2H, dd, *J* 7.1 and 6.9, 3-CH_2), 1.97 (2H, td, *J* 7.2 and 6.8, 6-CH_2), 1.40–1.28 (2H, m, 7-CH_2), 1.20 (3H, d, *J* 6.6, 1-Me) and 0.87 (3H, t, *J* 7.2, 8-Me); *m/z* (FAB) 224 (M^+ + 1, 9%), 209 (12), 197 (34), 135 (100), 109 (59), 83 (29) and 69 (94) [Found: M^+ + 1, 224.1272. $C_{10}H_{17}F_3NO$ requires *M*, 224.1262].

(*E*)-2-Acetylaminooct-4-ene 35d. A solution of amine **35b** (0.10 g, 0.78 mmol), acetic anhydride (0.07 ml, 0.78 mmol), triethylamine (0.11 ml, 0.78 mmol) and 4-dimethylaminopyridine (10 mg) in dichloromethane (10 ml) was stirred at ambient temperature for 18 h. The reaction mixture was then neutralised with 2 M hydrochloric acid and extracted with dichloromethane (3 × 10 ml). The combined organic solutions were dried and evaporated to afford the *amide* **35d** (0.92 g, 70%) as a pale yellow oil: R_f 0.52 (methanol–dichloromethane 1 : 9); ν_{max}/cm^{-1} 3454 (NH), 2956 (s), 2932 (s), 1682 (C=O), 1430 (s) and 1351 (s); δ_H (270) 5.39 (1H, dt, *J* 15.5 and 6.6, 5-H), 5.23 (1H, dt, *J* 15.5 and 6.3, 4-H), 3.83–3.99 (1H, m, 2-H), 2.04 (2H, dd, *J* 6.6 and 6.3, 3-CH_2), 1.91 (2H, td, *J* 7.2 and 6.6, 6-CH_2), 1.85 (3H, s, C(O)Me), 1.27 (2H, hex, *J* 7.2, 7-CH_2), 1.03 (2H, d, *J* 6.6, 1-Me) and 0.79 (3H, t, *J* 7.2, 8-Me); δ_C (67.8) 169.8 (C(O)Me), 134.1, 125.5 (both =CH), 44.9 (2-CH), 39.5, 34.7 (both CH_2), 24.3 (C(O)Me), 22.6 (CH_2), 20.2 (1-Me) and 13.6 (8-Me); *m/z* (FAB) 170 (M^+ + 1, 24%), 155 (30), 154 (100), 136 (70), 107 (25) and 77 (21).

(*E*)-2-Methoxycarbonylaminooct-4-ene 35e. A solution of amine **35b** (0.10 g, 0.78 mmol), methyl chloroformate (0.06 ml, 0.86 mmol, freshly distilled from calcium hydride) and triethylamine (0.12 ml, 0.86 mmol) in dichloromethane (20 ml) was stirred at ambient temperature for 5 h then neutralised with 2 M hydrochloric acid and extracted with dichloromethane (3 × 20 ml). The combined organic solutions were dried and evaporated to give a mixture of mono- and diacylated products which were separated by cc (methanol–dichloromethane 5 : 95) to afford the *carbamate* **35e** (0.08 g, 53%) as a pale yellow oil: R_f 0.14 (dichloromethane); ν_{max}/cm^{-1} 3437 (NH), 2961 (s), 2931 (s), 1713 (C=O), 1514 (s) and 1435 (s); δ_H (270) 5.55–5.31 (2H, m, 4- and 5-H), 3.92–3.79 (1H, m, 2-H), 3.62 (3H, s, OMe), 2.11 (2H, dd, *J* 6.5 and 6.2, 3-CH_2), 1.95 (2H, td, *J* 7.3 and 6.6, 6-CH_2), 1.35 (2H, hex, *J* 7.3, 7-CH_2), 1.15 (3H, d, *J* 6.6, 1-Me) and 0.89 (3H, t, *J* 7.3, 8-Me); δ_C (67.8) 156.2 (*C*(O)OMe), 134.6, 124.9 (both =CH), 54.6 (C(O)O*M*e), 47.0 (2-CH), 43.7, 34.6, 22.5 (all CH_2), 20.1 (1-Me) and 13.6 (8-Me) [Found (ES): M^+ + 1, 186.1491. $C_{10}H_{20}NO_2$ requires *M*, 186.1494].

Iodocyclisations with sodium hydrogen carbonate as base: general procedure

To a stirred mixture of the cyclisation precursor (1 mmol, 1 eq.) and sodium hydrogen carbonate (0.25 g, 3 mmol, 3 eq.) in dry acetonitrile (1 ml) was added portionwise iodine (0.76 g, 3 mmol, 3 eq.). The reaction mixture was stirred at ambient temperature until no starting material remained according to TLC analysis (typically 5–30 min). The reaction mixture was then treated with saturated aqueous sodium thiosulfate (1–2 ml) and the resulting pale yellow solution extracted with dichloromethane (3 × 2 ml). The combined organic solutions were dried, filtered and the solvent evaporated to yield the crude product which was purified by column chromatography. Any isomer ratios quoted were determined from ^{1}H NMR spectra for the mixtures; the peaks used for the determination of the ratios are stated in each case.

Cyclisation of 4-(phenylsulfonylamino)pent-1-ene 24a. Homoallylic sulfonamide **24a** (0.06 g, 0.25 mmol) was reacted under the conditions described above for 1 h. The crude product was purified by cc (dichloromethane) to afford an inseparable mixture of isomers in the ratio 3 : 2 together with a trace of another unidentified product (0.04 g, 42%). The isomer ratio was determined by measurement of the alkyl methyl peaks. Data for the two predominant isomers: R_f 0.55 (hexane–ethyl acetate 1 : 1); δ_H (250) 7.79–7.91 (4H, m, Ar-H, both isomers), 7.65–7.51 (6H, m, Ar-H, both isomers), 3.93–3.84 (1H, m, minor isomer), 3.79–3.64 (3H, m, both isomers), 3.61–3.50 (2H, m, both isomers), 3.46–3.38 (1H, m, minor isomer), 3.28–3.17 (2H, m, major isomer), 2.62–2.50 (1H, m, minor isomer), 2.31–2.19 (1H, m, major isomer), 1.99–1.84 (1H, m, minor isomer), 1.61–1.52 (1H, m, major isomer), 1.38 (3H, d, *J* 5.9, minor isomer) and 1.32 (3H, d, *J* 6.3, major isomer); δ_C (100) 138.4 (Ar-C,

minor isomer), 135.8 (Ar-C, major isomer), 133.4 (Ar-CH, minor isomer), 129.4 (Ar-CH, minor isomer), 129.3 (Ar-CH, major isomer), 129.2 (Ar-CH, minor isomer), 128.3 (Ar-CH, major isomer), 127.4 (Ar-CH, major isomer), 59.8 (CH, major isomer), 58.6 (CH_2, minor isomer), 56.8 (CH, minor isomer), 55.5 (CH, major isomer), 46.7 (CH_2, minor isomer), 32.6 (CH_2 major isomer), 22.6 (Me, minor isomer), 22.3 (Me, major isomer) and 10.2 (CH_2, major isomer); *m*/*z* (EI) 351 (M^+, 2%), 336 ($M^+ - Me$, 30%), 224 (25), 210 (96), 141 (74) and 77 (100) [$C_{11}H_{14}INO_2S$ requires *M*, 351].

(2*SR*,3*RS*)-2-Ethyl-3-iodo-1-(*p*-tolylsulfonyl)pyrrolidine 36b. (*E*)-Homoallylic tosylamide **24b** (0.20 g, 0.79 mmol) was cyclised under the general conditions above, and the reaction was complete within 10 min. The crude product was obtained as a colourless solid, which was recrystallised (hexane–ethyl acetate 9 : 1) to give the *iodopyrrolidine* **36b** (0.25 g, 84%) as a colourless, crystalline solid, mp 109–110 °C: R_f 0.52 (dichloromethane); ν_{max}/cm^{-1} ($CHCl_3$) 2950 (s), 2923 (s), 2856 (w), 1592 (w), 1456 (w) and 1338 (s); δ_H (400) 7.75 (2H, d, *J* 8.3, Ar-H), 7.32 (2H, d, *J* 8.3, Ar-H), 4.14 (1H, ddd, *J* 5.1, 2.1 and 1.4, 3-H), 3.88 (1H, ddd, *J* 9.5, 3.9 and 1.4, 2-H), 3.55 (1H, ddd, *J* 9.8, 7.2 and 2.5, 5-H_α), 3.42 (1H, ddd, *J* 9.8, 9.8 and 6.2, 5-H_β), 2.41 (3H, s, Ar-Me), 2.25 (1H, dddd, *J* 14.0, 9.8, 5.1 and 2.5, 4-H_α), 1.95 (1H, dddd, 14.0, 7.2, 6.2 and 2.1, 4-H_β), 1.83 (1H, dqd, *J* 9.5, 7.5 and 3.9, 1′-H_α), 1.46 (1H, ddq, *J* 9.5, 9.5 and 7.5, 1′-H_β) and 0.96 (3H, t, *J* 7.5, 2′-Me); δ_C (100) 143.1, 132.6 (both Ar-C), 129.5, 127.8 (both Ar-CH), 72.9 (2-CH), 47.6 (5-CH_2), 35.9 (4-CH_2), 30.3 (1′-CH_2), 23.8 (Ar- Me), 21.4 (3-CH) and 10.1 (2′-Me); *m*/*z* (ES) 380 ($M^+ + 1$, 100%), 329 (7), 279 (8), 254 (20), 83 (12) and 60 (23) [Found: $M^+ + 1$, 380.0181. $C_{13}H_{19}INO_2S$ requires *M*, 380.0187].

(2*SR*,3*RS*)-1-Phenylsulfonyl-2-ethyl-3-iodopyrrolidine 36c. (*E*)-Homoallylic sulfonamide **24c** (0.20 g, 0.84 mmol) was cyclised under the general conditions described above and the reaction was complete within 10 min. The crude product was obtained as a colourless solid, which was recrystallised (hexane–ethyl acetate 9 : 1) to afford the *iodopyrrolidine* **36c** (0.26 g, 84%) as a colourless crystalline solid, mp 101–102 °C: R_f 0.56 (dichloromethane); $\nu_{max}\,cm^{-1}$/($CHCl_3$) 2951 (s), 2920 (s), 2856 (w), 1592 (w), 1452 (s) and 1338 (s); δ_H (400) 7.93–7.53 (5H, m, Ph), 4.17 (1H, ddd, *J* 5.2, 2.1 and 1.4, 3-H), 3.90 (1H, ddd, *J* 9.4, 3.8 and 1.4, 2-H), 3.62 (1H, ddd, *J* 9.8, 7.2 and 2.5, 5-H_α), 3.43 (1H, ddd, *J* 9.8, 9.8 and 6.2, 5-H_β), 2.27 (1H, dddd, *J* 14.0, 9.8, 7.2 and 5.2, 4-H_α), 1.96 (1H, dddd, 14.0, 6.2, 2.5 and 2.1, 4-H_β), 1.83 (1H, dqd, *J* 14.0, 7.5 and 3.8, 1′-H_α), 1.46 (1H, ddq, *J* 14.0, 9.4 and 7.5, 1′-H_β) and 0.98 (3H, t, *J* 7.5, 2′-Me); δ_C (100) 136.3 (Ar-C), 132.9, 129.5, 127.8 (all Ar-CH), 73.1 (2-CH), 47.7 (5-CH_2), 35.9 (4-CH_2), 30.8 (1′-CH_2), 23.8 (3-CH) and 10.2 (2′-Me); *m*/*z* (EI) 336 ($M^+ - C_2H_5$, 28%), 208 (39), 141 (65), 128 (63), 86 (98) and 77 (100) [Found: C, 39.6; H, 4.5; N, 3.8. $C_{12}H_{16}INO_2S$ requires C, 39.5; H, 4.4; N, 3.8%].

(2*SR*,3*RS*,5*SR*)- and (2*RS*,3*SR*,5*SR*)-2-Butyl-5-ethyl-3-iodo-1-(*p*-tolylsulfonyl)pyrrolidine 36f and 37f. (*E*)-Homoallylic sulfonamide **24f** (0.05 g, 0.16 mmol) was cyclised under the general conditions described above; the reaction was complete after 25 min. The resulting crude oil was purified by cc (dichloromethane) to yield the *iodopyrrolidine* as a yellow oil (0.05 g, 76%) in a ratio of isomers of 3 : 1. The isomer ratio was determined by measurement of the aryl-methyl peaks in the ^1H NMR spectrum. Comparison of the spectral data for the mixture with those for the potassium carbonate and base-free reactions (see later) revealed that the major isomer was the 2,5-*trans*-pyrrolidine **36f** while the minor product was the 2,5-*cis*-pyrrolidine **37f**.

(2*SR*,3*RS*,5*SR*)- and (2*RS*,3*SR*,5*SR*)-5-Ethyl-3-iodo-2-phenyl-1-(*p*-tolylsulfonyl)pyrrolidine 36j and 37j. (*E*)-Homoallylic tosylamide **24j** (0.04 g, 0.12 mmol) was subjected to the iodocyclisation conditions described in the general procedure and the reaction was complete after 40 min. The resulting crude product was purified by cc (dichloromethane) to yield the title compounds as a colourless solid (0.04 g, 76%) in an isomer ratio of 2 : 1. The isomer ratio was measured by comparison of the aryl-methyl peaks in the ^1H NMR spectrum. Comparison of the spectral data (see below) for the mixture with those for the potassium carbonate and base-free reactions showed that the major isomer was the 2,5-*trans*-pyrrolidine **36j** and the minor isomer was the corresponding 2,5-*cis*-pyrrolidine **37j**.

Cyclisation of (*Z*)-1-(*p*-tolylsulfonylamino)hex-3-ene 26a. (*Z*)-Homoallylic tosylamide **26a** (0.20 g, 0.79 mmol) was reacted under the general conditions described above and the reaction appeared complete after 1 h. The crude product was obtained as a yellow oil, which was purified by cc (dichloromethane) to give an inseparable mixture of isomers (0.12 g, 40%) in the ratio 2 : 1. The isomer ratio was determined by measurement of the signals corresponding to the alkyl methyl groups in the ^1H NMR spectrum. Comparison of the ^1H NMR spectrum with that for iodocyclisation of the corresponding (*E*)-tosylamide **24b** revealed that the minor product was the 2,3-*trans*-iodopyrrolidine **36b** (see above). Data for mixture: R_f 0.52 (dichloromethane); δ_H (270) 7.80–7.73 (4H, m, Ar-H, both isomers), 7.45–7.30 (4H, m, Ar-H, both isomers), 4.20–4.04 (2H, m, both isomers), 3.89–3.70 (2H, m, both isomers), 3.55–2.95 (4H, m, both isomers), 2.41 (3H, s, Ar-Me, minor isomer), 2.38 (3H, s, Ar-Me, major isomer), 2.27–1.39 (8H, m, both isomers), 1.04 (3H, t, *J* 7.3, major isomer) and 0.96 (3H, t, *J* 7.5, 2′-Me, minor isomer).

Cyclisation of (*Z*)-1-(methylsulfonylamino)hex-3-ene 26b. (*Z*)-Homoallylic mesylamide **26b** (0.02 g, 0.07 mmol) in acetonitrile (0.2 ml) was reacted as described in the general procedure for 1 h. The crude product was purified by cc (dichloromethane) to give an inseparable mixture of isomers in the ratio 1 : 1 (0.06 g, 45%). The ratio of isomers was determined by integration of the –SO_2Me peaks in the ^1H NMR spectrum. Data for the mixture: R_f 0.53 (dichloromethane); δ_H (250) 4.79–4.68 (1H, m), 4.31–4.20 (1H, m), 4.08–3.96 (1H, m), 3.62–3.15 (4H, m), 3.00 (3H, s, SO_2Me), 2.98 (3H, s, SO_2Me), 2.11–1.34 (8H, m), 1.06 (3H, t, *J* 7.3, Me) and 0.97 (3H, t, *J* 7.3, Me).

Cyclisation of (*Z*)-3-(*p*-tolylsulfonylamino)dec-5-ene 26c. (*Z*)-Homoallylic tosylamide **26c** (0.10 g, 0.34 mmol) was cyclised under the conditions described in the general procedure above for 1 h. The crude product was purified by cc (dichloromethane) and gave an inseparable mixture of isomers in the ratio 3 : 2 : 2 (0.09 g, 65%). The two minor isomers were found (by comparison of ^1H NMR data for the mixture) to be identical to the products (**36f** and **37f**) obtained from the cyclisation of the corresponding (*E*)-homoallylic tosylamide **24f** (see above). The major isomer was tentatively assigned the all-*cis*-structure **44**.

Potassium carbonate as base: general procedure

A mixture of the cyclisation precursor (1.0 mmol, 1 eq.) and potassium carbonate (0.41 g, 3 mmol, 3 eq.) in dry acetonitrile (1 ml) and water (0.01 ml) was stirred for 0.5 h, after which time iodine (0.76 g, 3 mmol, 3 eq.) was added portionwise. The reaction was followed by TLC analysis, and once complete (typically 0.5–1 h), the mixture was quenched with saturated aqueous sodium thiosulfate (1 ml). The resulting layers were separated and the aqueous layer extracted with dichloromethane (3 × 2 ml). The combined organic solutions were dried and evaporated to yield the crude product which was purified by column chromatography.

(2*SR*,3*RS*)-2-Ethyl-3-iodo-1-(*p*-tolylsulfonyl)pyrrolidine 36b. (*E*)-Homoallylic sulfonamide **24b** (0.20 g, 0.79 mmol) was cyclised under the conditions described above using potassium carbonate as the base, and the reaction was complete after 20 min. The crude product was purified by recrystallisation (hexane–ethyl acetate 9 : 1) to yield the *iodopyrrolidine* **36b** (0.22 g, 73%) as a colourless crystalline solid, mp 108–110 °C; other spectral and analytical data were identical to the sample prepared using sodium hydrogen carbonate as the base (see above).

(2*SR*,3*RS*,5*SR*)-2-Butyl-3-iodo-5-methyl-1-(*p*-tolylsulfonyl)-pyrrolidine 36d. (*E*)-Homoallylic tosylamide **24d** (0.20 g, 0.68 mmol) was subjected to the cyclisation conditions described in the general procedure (K_2CO_3), and the reaction was complete after 25 min. The resulting crude product was purified by cc (dichloromethane) then recrystallised (hexane–ethyl acetate 9 : 1) to afford the *iodopyrrolidine* **36d** (0.24 g, 85%) as a colourless, crystalline solid, mp 84–85 °C: R_f 0.52 (dichloromethane); ν_{max}/cm^{-1} ($CHCl_3$) 2957 (s), 2928 (s), 2856 (w), 1597 (w), 1458 (s) and 1335 (s); δ_H (250) 7.84 (2H, d, *J* 8.3, Ar-H), 7.30 (2H, d, *J* 8.3, Ar-H), 4.29–4.20 (2H, m, 2- and 3-H), 4.15 (1H, dqd, *J* 9.0, 6.6 and 3.0, 5-H), 2.89 (1H, ddd, *J* 15.2, 9.0 and 6.1, 4-H_α), 2.43 (3H, s, Ar-Me), 2.10 (1H, ddd, *J* 15.2, 3.0 and 3.0, 4-H_β), 2.05–1.98 (2H, m, 1′-CH_2), 1.42 (3H, d, *J* 6.6, 5-Me), 1.37–1.21 (4H, m, 2′- and 3′-CH_2) and 0.91 (3H, t, *J* 6.9, 4′-Me); δ_C (67.8) 142.8, 139.6 (both Ar-C), 129.5, 126.9 (both Ar-CH), 74.3 (2-CH), 55.2 (5-CH), 43.2 (4-CH_2), 34.4 (1′-CH_2), 28.2 (2′-CH_2), 22.3 (3′-CH_2), 22.0 (5-Me), 21.3 (3-CH), 21.2 (Ar-Me) and 13.8 (4′-Me); *m*/*z* (FAB) 422 (M^+ + 1, 68%), 391 (7), 364 (39), 294 (47), 198 (100), 155 (69), 136 (56), 91 (86) and 77 (30) [Found: C, 45.7; H, 6.0; N, 3.6; M^+ + 1, 422.0596. $C_{16}H_{24}INO_2S$ requires C, 45.6; H, 5.7; N, 3.3%; $C_{16}H_{25}INO_2S$ requires *M*, 422.0566].

(2*SR*,3*RS*,5*SR*)-2-Butyl-5-ethyl-3-iodo-1-(*p*-tolylsulfonyl)-pyrrolidine 36f. (*E*)-Homoallylic tosylamide **24f** (0.20 g, 0.64 mmol) was cyclised under the conditions described in the general procedure (K_2CO_3) and the reaction was complete after 30 min. The crude product was purified by cc (dichloromethane) then recrystallised (hexane–ethyl acetate 9 : 1) to yield the *title compound* **36f** (0.21 g, 74%) as a colourless, crystalline solid: mp 72–73 °C; R_f 0.52 (dichloromethane); ν_{max}/cm^{-1} ($CHCl_3$) 2950 (s), 2927 (s), 2872 (w), 1465 (w), 1337 (s); δ_H (400) 7.82 (2H, d, *J* 8.3, Ar-H), 7.29 (2H, d, *J* 8.3, Ar-H), 4.27–4.19 (2H, m, 2- and 3-H), 3.86 (1H, dddd, *J* 11.2, 8.7, 3.3 and 3.2, 5-H), 2.73 (1H, ddd, *J* 15.2, 8.7 and 6.6, 4-H_α), 2.41 (3H, s, Ar-Me), 2.25 (1H, ddd, *J* 15.2, 3.2 and 2.2, 4-H_β), 2.09–1.50 (4H, m, 1′- and 1″-CH_2), 1.47–1.28 (4H, m, 2′- and 3′-CH_2), 0.88 (3H, t, *J* 7.2, 2″-Me) and 0.79 (3H, t, *J* 7.4, 4′-Me); δ_H (d_6-acetone, 400) 7.85 (2H, d, *J* 8.3, Ar-H), 7.37 (2H, d, *J* 8.3, Ar-H), 4.48 (1H, ddd, *J* 6.6, 2.2 and 1.6, 3-H), 4.23 (1H, ddd, *J* 10.1, 3.2 and 1.6, 2-H), 3.89 (1H, dddd, *J* 11.2, 8.7, 3.3 and 3.2, 5-H), 2.88 (1H, ddd, *J* 15.3, 8.7 and 6.6, 4-H_α), 2.59 (3H, s, Ar-Me), 2.23 (1H, ddd, *J* 15.3, 3.2 and 2.2, 4-H_β), 2.20–1.95 (2H, m, 1′-CH_2), 1.72 (1H, ddq, *J* 14.1, 11.2 and 7.3, 1″-H_α), 1.49 (1H, dqd, *J* 14.1, 7.3 and 3.3, 1″-H_β), 1.47–1.15 (4H, m, 2′- and 3′-CH_2), 0.92 (3H, t, *J* 7.3, 2″-Me) and 0.86 (3H, t, *J* 7.5, 4′-Me); δ_C (67.8) 142.9, 139.6 (both Ar-C), 129.3, 127.0 (both Ar-CH), 74.2 (2-CH), 61.4 (5-CH), 39.3 (4-CH_2), 34.5 (1′-CH_2), 31.5 (1″-CH_2), 26.4, 25.9 (both CH_2), 21.4 (3-CH), 21.3 (Ar-Me), 13.9 (4′-Me) and 10.9 (2″-Me); *m*/*z* (ES) 436 (M^+ + 1), 391 (10), 102 (28), 83 (72) and 60 (100) [Found C, 46.9; H, 6.15; N, 3.3. $C_{17}H_{26}INO_2S$ requires C, 46.9; H, 6.0; N, 3.3%].

(2*SR*,3*RS*,5*SR*)-2-Butyl-5-ethyl-3-iodo-1-methylsulfonyl-pyrrolidine 36g. (*E*)-Homoallylic sulfonamide **24g** (0.01 g, 0.04 mmol) in acetonitrile (0.2 ml) was cyclised under the conditions described in the general procedure (K_2CO_3) and the reaction was complete after 25 min. The resulting crude product was purified by cc (dichloromethane) to afford the *iodopyrrolidine* **36g** (0.01 g, 72%) as a pale yellow, viscous oil: R_f 0.59 (dichloromethane); ν_{max}/cm^{-1} 2952 (s), 2931 (s), 2875 (w), 1461 (w) and 1341 (s); δ_H (400) 4.29 (1H, ddd, *J* 6.3, 2.3 and 1.7, 3-H), 4.05 (1H, ddd, *J* 10.3, 3.3 and 1.7, 2-H), 3.88 (1H, dddd, *J* 11.9, 9.0, 3.2 and 2.9, 5-H), 3.06 (3H, s, SO_2Me), 2.41–2.29 (2H, m, 1′-CH_2), 2.74 (1H, ddd, *J* 15.3, 9.0 and 6.3, 4-H_α), 2.32 (1H, ddd, *J* 15.3, 3.2 and 2.3, 4-H_β), 2.09 (1H, ddq, *J* 15.0, 11.9 and 7.3, 1″-H_α), 1.43 (1H, dqd, *J* 15.0, 7.3 and 2.9, 1″-H_β), 1.38–1.24 (4H, m, 2′- and 3′-CH_2), 0.95 (3H, t, *J* 7.3, 2″-Me) and 0.88 (3H, t, *J* 7.5, 4′-Me); δ_C (67.8) 73.9 (2-CH), 61.4 (5-CH), 42.4 (SO_2Me), 38.5 (4-CH_2), 35.2 (1″-CH_2), 28.4, 26.2, 22.5 (all CH_2), 22.1 (3-CH), 13.9 (2″-Me) and 11.1 (4′-Me); *m*/*z* (ES) 360 (M^+ + 1, 38%), 254 (36), 234 (39), 193 (30), 83 (66) and 64 (100) [Found: M^+ + 1, 360.0494. $C_{11}H_{23}INO_2S$ requires *M*, 360.0499].

(2*SR*,3*RS*,5*SR*)-5-Ethyl-3-iodo-2-pentyl-1-(*p*-tolylsulfonyl)-pyrrolidine 36h. (*E*)-Homoallylic sulfonamide **24h** (0.05 g, 0.16 mmol) in acetonitrile (0.3 ml) was cyclised under the conditions described in the general procedure (K_2CO_3) and the reaction was complete after 25 min. The resulting crude product was purified by cc (dichloromethane) to yield the *title compound* **36h** (0.06 g, 79%) as a pale yellow, viscous oil: R_f 0.49 (dichloromethane); ν_{max}/cm^{-1} 2952 (s), 2931 (s), 2875 (w), 1461 (w) and 1342 (s); δ_H (400) 7.84 (2H, d, *J* 8.3, Ar-H), 7.28 (2H, d, *J* 8.3, Ar-H), 4.29–4.21 (2H, m, 2- and 3-H), 3.85 (1H, dddd, *J* 11.3, 8.8, 3.2 and 3.1, 5-H), 2.71 (1H, ddd, *J* 15.2, 8.8 and 6.6, 4-H_α), 2.42 (3H, s, Ar-Me), 2.25 (1H, ddd, *J* 15.2, 3.2 and 2.2, 4-H_β), 2.09–1.50 (4H, m, 1′- and 1″-CH_2), 1.49–1.16 (6H, m, 2′-, 3′- and 4′-CH_2), 0.94 (3H, t, *J* 6.9, 2″-Me) and 0.88 (3H, t, *J* 7.5, 5′-Me); δ_C (67.8) 142.9, 140.0 (both Ar-C), 129.3, 127.0 (both Ar-CH), 74.2 (2-CH), 61.4 (5-CH), 39.3, 34.5, 31.5, 26.4, 25.9, 22.4 (all CH_2), 21.5 (3-CH), 21.3 (Ar-Me), 13.9 (11-Me) and 11.0 (1-Me) [Found: C, 48.3; H, 6.3; N 3.1. $C_{18}H_{28}INO_2S$ requires C, 48.1; H, 6.2; N, 3.1%].

(2*SR*,3*RS*,5*SR*)-5-Butyl-3-iodo-2-pentyl-1-(*p*-tolylsulfonyl)-pyrrolidine 36i. (*E*)-Homoallylic sulfonamide **24i** (0.30 g, 0.85 mmol) was cyclised under the general conditions (K_2CO_3), and the reaction was complete after 35 min. The resulting crude product was purified by cc (dichloromethane) to yield the *title compound* **36i** (0.33 g, 78%) as a viscous, pale yellow oil: R_f 0.62 (dichloromethane); ν_{max}/cm^{-1} 2950 (s), 2935 (s), 2871 (w), 1461 (w), 1358 (s) and 1342 (s); δ_H (400) 7.82 (2H, d, *J* 8.3, Ar-H), 7.29 (2H, d, *J* 8.3, Ar-H), 4.24–4.19 (2H, m, 2- and 3-H), 3.94 (1H, dddd, *J* 11.2, 8.7, 3.4 and 3.2, 5-H), 3.71 (1H, ddd, *J* 15.2, 8.7 and 6.6, 4-H_α), 2.42 (3H, s, Ar-Me), 2.20 (1H, ddd, *J* 15.2, 3.4 and 2.3, 4-H_β), 2.06–2.01 (2H, m, 1′-CH_2), 1.71–1.61 (2H, m, 1″-CH_2), 1.61–1.11 (10H, m, 2′-, 2″-, 3′-, 3″- and 4′-CH_2), 0.89 (3H, t, *J* 7.2, Me) and 0.83 (3H, t, *J* 7.1, Me); δ_C (67.8) 142.9, 139.9 (both Ar-C), 129.0, 127.0 (both Ar-CH), 73.9 (2-CH), 60.0 (5-CH), 39.8 (4-CH_2), 34.4 (1′-CH_2), 33.0 (1″-CH_2), 31.6, 29.4, 26.8, 22.5, 22.4 (all CH_2), 21.6 (3-CH), 21.4 (Ar-Me), 13.9 (Me) and 13.8 (Me); *m*/*z* (ES) 478 (M^+ + 1, 100%), 391 (5), 254 (96) and 60 (7) [Found: M^+ + 1, 478.1280. $C_{20}H_{33}INO_2S$ requires *M*, 478.1279].

(2*SR*,3*RS*,5*SR*)-5-Ethyl-3-iodo-2-phenyl-1-(*p*-tolylsulfonyl)-pyrrolidine 36j. (*E*)-Homoallylic tosylamide **24j** (1.00 g, 3.04 mmol) was subjected to the iodocyclisation conditions described in the general procedure (K_2CO_3), and the reaction was complete after 45 min. The resulting orange solid was purified by cc (dichloromethane) followed by recrystallisation (hexane–ethyl acetate 9 : 1) to afford the *2-phenyliodopyrrolidine* **36j** (1.12 g, 83%) as a pale cream solid: mp 156–157 °C; R_f 0.52 (dichloromethane); ν_{max}/cm^{-1}($CHCl_3$) 3286 (s), 3062 (s), 2966 (s), 2876 (w), 2251 (w), 1700 (w), 1676 (w) and 1446 (s); δ_H (400) 7.59 (2H, d, *J* 8.3, Ar-H), 7.31–7.16 (7H, m, Ar-H), 5.32 (1H, d, *J* 2.3, 2-H), 4.28–4.18 (2H, m, 3- and 5-H), 2.74 (1H, ddd, *J* 15.0, 8.7 and 6.7, 4-H_α), 2.40 (3H, s, Ar-Me), 2.25

(1H, ddd, *J* 15.0, 3.0 and 2.4, 4-H_β), 1.98–1.84 (2H, m, 1′-CH_2) and 0.91 (3H, t, *J* 7.4, 2′-Me); δ_H (270, d_6-benzene) 8.05–7.13 (9H, m, Ar-H), 5.70 (1H, d, *J* 2.3, 2-H), 4.28 (1H, dddd, *J* 11.2, 8.3, 3.3 and 3.2, 5-H), 3.98 (1H, ddd, *J* 6.6, 3.3 and 2.3, 3-H), 2.72 (1H, ddd, *J* 14.8, 11.2 and 6.6, 4-H_α), 2.62 (3H, s, Ar-Me), 2.31–2.19 (2H, m, 1′-CH_2), 2.10 (1H, ddd, *J* 14.8, 3.3 and 3.3, 4-H_β) and 0.93 (3H, t, *J* 7.3, 2′-Me); δ_C (100) 143.7, 140.4, 134.5 (all Ar-C), 129.6, 128.5, 128.0, 127.9, 126.6 (all Ar-CH), 74.8 (2-CH), 62.9 (5-CH), 41.8 (4-CH_2), 28.7 (1′-CH_2), 26.2 (3-CH), 21.6 (Ar-Me) and 10.7 (2′-Me); *m*/*z* (ES) 456 (M^+ + 1, 100%), 282 (10), 276 (47) and 104 (21) [Found: C, 50.2; H, 5.0; N, 3.1. $C_{19}H_{22}INO_2S$ requires C, 50.1; H, 4.9; N, 3.1%].

(2*SR*,3*RS*,4*SR*,5*RS*)-4,5-Dimethyl-3-iodo-2-propyl-1-(*p*-tolylsulfonyl)pyrrolidine 38. (*E*)-*anti*-Homoallylic tosylamide **27b** (0.20 g, 0.7 mmol) was subjected to the iodocyclisation conditions described above (K_2CO_3) and the reaction was complete after 40 min. The resulting crude product was purified by cc (dichloromethane) followed by recrystallisation (hexane–ethyl acetate 9 : 1) to yield the *iodopyrrolidine* **38** (0.22 g, 76%) as a colourless, crystalline solid, mp 102–103 °C: R_f 0.62 (dichloromethane); ν_{max}/cm^{-1}($CHCl_3$) 2950 (s), 2932 (s), 2873 (w), 1462 (w) and 1339 (s); δ_H (400) 7.72 (2H, d, *J* 8.2, Ar-H), 7.33 (2H, d, *J* 8.2, Ar-H), 3.87 (1H, ddd, *J* 8.7, 6.2 and 3.6, 2-H), 3.72 (1H, dq, *J* 7.2 and 6.9, 5-H), 3.61 (1H, dd, *J* 11.6 and 8.7, 3-H), 2.45 (3H, s, Ar-Me), 1.95–1.89 (2H, m, 1′-CH_2), 1.60 (1H, ddq, 11.6, 7.2 and 6.8, 4-H), 1.48–1.36 (2H, m, 2′-CH_2), 1.11 (3H, d, *J* 6.9, 5-Me), 0.97 (3H, t, *J* 7.2, 3′-Me) and 0.99 (3H, d, *J* 6.8, 4-Me); δ_C (67.8) 143.6, 134.6 (both Ar-C), 129.8, 127.4 (both Ar-CH), 69.4 (2-CH), 58.6 (5-CH), 46.5 (4-CH), 35.9 (1′-CH_2), 30.5 (3-CH), 21.6 (Ar-Me), 17.67 (2′-CH_2), 17.2 (5-Me), 14.2 (3′-Me) and 12.7 (4-Me); *m*/*z* (FAB) 422 (M^+ + 1, 36%), 378 (13), 294 (28), 251 (8), 198 (37), 155 (29), 123 (16), 109 (24), 91 (52) and 69 (90) [Found: C, 46.0; H, 5.7; N, 3.0; M^+ + 1, 422.0618. $C_{16}H_{24}INO_2S$ requires C, 45.6; H, 5.8; N, 3.3%; $C_{16}H_{25}INO_2S$ requires *M*, 422.0650].

(2*RS*,3*SR*,4*RS*,5*RS*)-4,5-Dimethyl-3-iodo-2-propyl-1-(*p*-tolylsulfonyl)pyrrolidine 39. (*E*)-*syn*-Homoallylic tosylamide **28b** (0.20 g, 0.7 mmol) was cyclised under the conditions described in the general procedure (K_2CO_3), and the reaction was complete after 45 min. The crude product was purified by cc (dichloromethane) to yield the *iodopyrrolidine* **39** (0.23 g, 79%) as a colourless crystalline solid, mp 108–109 °C: R_f 0.64 (dichloromethane); ν_{max}/cm^{-1} ($CHCl_3$) 2953 (s), 2928 (s), 2879 (w), 1458 (w) and 1345 (s); δ_H (250) 7.75 (2H, d, *J* 8.3, Ar-H), 7.28 (2H, d, *J* 8.3, Ar-H), 4.31 (1H, ddd, *J* 7.6, 6.3 and 4.1, 2-H), 3.50 (1H, dd, *J* 9.2 and 6.3, 3-H), 3.20 (1H, dq, *J* 9.4 and 6.5, 5-H), 2.42 (3H, s, Ar-Me), 2.10–1.95 (2H, m, 1′-CH_2), 1.71 (1H, ddq, *J* 9.4, 9.2 and 6.6, 4-H), 1.49–1.38 (2H, m, 2′-CH_2), 1.31 (3H, d, *J* 6.5, 5-Me), 0.97 (3H, d, *J* 6.6, 4-Me) and 0.94 (3H, t, *J* 7.3, 3′-Me); δ_C (67.8) 143.0, 141.3 (both Ar-C), 129.6, 126.5 (both Ar-CH), 70.6 (2-CH), 61.8 (5-CH), 52.8 (4-CH), 36.8 (1′-CH_2), 30.3 (3-CH), 21.5 (Ar-Me), 18.3 (2′-CH_2), 16.8 (5-Me), 15.2 (4-Me) and 14.1 (3′-Me); *m*/*z* (FAB) 422 (M^+ + 1, 1%), 421 (M^+, 39%), 378 (13), 294 (28), 279 (5), 251 (8), 198 (29), 155 (29), 91 (60), 71 (44) and 69 (100) [Found: C, 45.7; H, 5.9; N, 3.0%; M^+, 421.0595. $C_{16}H_{24}INO_2$ requires *M*, 421.0574].

Cyclisation of (*Z*)-1-(*p*-tolylsulfonylamino)hex-3-ene 26a. (*Z*)-Homoallylic tosylamide **26a** (0.02 g, 0.07 mmol) in acetonitrile (0.2 ml) was reacted under the conditions described in the general procedure (K_2CO_3) for 1 h. Purification of the crude product by cc (dichloromethane) afforded a mixture of isomers in a ratio 2 : 1 (0.01 g, 52%). The isomer ratio was determined from measurement of the alkyl methyl peaks from the ^1H NMR spectrum. Data for mixture: R_f 0.58 (methanol–dichloromethane 2 : 98); δ_H (250) 7.75–7.72 (4H, m, Ar-H, both isomers), 7.32–7.29 (4H, m, Ar-H, both isomers), 5.01–4.85 (1H, m, minor isomer), 4.79–4.70 (1H, m, major isomer), 4.22–4.15 (1H, m, major isomer), 3.98–3.89 (1H, m, minor isomer), 3.21–1.95 (4H, m, both isomers), 2.38 (3H, s, Ar-Me, minor isomer), 2.36 (3H, s, Ar-Me, major isomer), 2.12–1.51 (8H, m, both isomers), 1.06 (3H, t, *J* 7.3, minor isomer) and 0.94 (3H, t, *J* 7.2, major isomer). These data indicate that the major isomer was the 2,3-*trans*-iodopyrrolidine **36b**.

Attempted cyclisation of (*Z*)-1-(methylsulfonylamino)hex-3-ene 26b. (*Z*)-Homoallylic mesylamide **26b** (0.02 g, 0.11 mmol) in acetonitrile (0.2 ml) was reacted under the conditions described above (K_2CO_3) for 1 h, but no reaction was observed. The reaction was repeated and left stirring for 24 h at ambient temperature but, again, no reaction was found to have occurred.

Cyclisation of (*Z*)-3-(*p*-tolylsulfonylamino)dec-5-ene 26c. (*Z*)-Homoallylic tosylamide **26c** (0.10 g, 0.33 mmol) was reacted under the conditions described above (K_2CO_3) for 1 h. The crude product was purified by cc (dichloromethane) to give an inseparable mixture of isomers in the ratio of *ca*. 5 : 1 (0.09 g, 63%). The isomer ratio was determined by integration of the aromatic methyl groups in the ^1H NMR spectrum. The major isomer was found, by comparison with spectral data from the cyclisation of the corresponding (*E*)-precursor **24f**, to be the foregoing (2*SR*,3*RS*,5*SR*)-iodopyrrolidine **36f** (see above). Data for the mixture: R_f 0.53 (dichloromethane); the minor isomer showed distinctive resonances at δ_H (250) 7.69 (2H, d, *J* 8.3, Ar-H), 7.38 (2H, d, *J* 8.3, Ar-H), 4.65–4.57 (1H, m), 4.42–4.32 (1H, m), 4.12–4.19 (1H, m) and 2.43 (3H, s, Ar-Me); comparisons with the spectral data displayed by the pyrrolidine **37f** suggested this was not the minor product which was hence assigned the all-*cis*-structure **44**.

Cyclisation of (*E*)-2-(*tert*-butoxycarbonylamino)oct-4-ene 35a. (*E*)-Homoallylic amide **35a** (0.03 g, 0.13 mmol) was reacted under the conditions described above (K_2CO_3) for 30 min. The crude product was purified by cc (methanol–dichloromethane 5 : 95) to afford the carbamate as a mixture of isomers **45** in the ratio 2 : 1 (0.04 g, 79%) as a viscous yellow oil: R_f 0.78 (methanol–dichloromethane 5 : 95); ν_{max}/cm^{-1} 3433 (NH), 3248 (NH), 2932 (w), 2874 (w), 1714 (C=O), 1459 (s) and 1342 (s); δ_H (250) 6.68 (1H, br s, NH, minor isomer), 6.52 (1H, br s, NH, major isomer), 4.31–3.98 (4H, m, both isomers), 3.70–3.51 (2H, m, both isomers), 2.41–2.15 (2H, m, minor isomer), 2.10–1.23 (10H, m, both isomers), 1.27 (3H, d, *J* 6.6, Me, minor isomer), 1.25 (3H, d. *J* 6.7, Me, major isomer), 0.90 (3H, t, *J* 7.3, Me, minor isomer) and 0.89 (3H, t, *J* 7.3, major isomer); δ_C (67.8) 154.3 (C=O, major isomer), 154.1 (C=O, minor isomer), 79.6 (CH, major isomer), 76.9 (CH, minor isomer), 46.3 (CH_2, major isomer), 43.8 (CH_2, minor isomer), 38.0 (CH, major isomer), 37.7 (CH_2, minor isomer), 37.6 (CH_2, major isomer), 37.2 (CH, minor isomer), 35.5 (CH_2, major isomer), 32.9 (CH_2, minor isomer), 29.1 (Me, minor isomer), 22.9 (CH_2, both isomers), 22.0 (Me, major isomer), 13.5 (Me, minor isomer) and 13.4 (Me, major isomer); *m*/*z* (FAB) 298 (M^+ + 1, 100%), 154 (48), 136 (54), 88 (67), 69 (56) and 55 (76) [Found: M^+ + 1, 298.0298. $C_9H_{17}INO_2$ requires *M*, 298.0304].

Cyclisation of (*E*)-2-trifluoroacetylaminooct-4-ene 35c. (*E*)-Homoallylic amide **35c** (0.05 g, 0.23 mmol) was reacted under the conditions described in the general procedure (K_2CO_3) for 1 h. The crude product was purified by cc (dichloromethane) to afford a mixture of isomers **46c** in a ratio of 3 : 1 (0.05g, 57%), as a yellow oil. The isomer ratio was determined by integration of the alkyl-methyl peaks in the ^1H NMR spectrum. Data for mixture: R_f 0.47 (dichloromethane); ν_{max}/cm^{-1} 2980 (s), 2951 (s), 1730, 1504 (s) and 1346 (s); δ_H (250) 4.12–4.09 (2H, m, major isomer), 4.01–3.97 (1H, m, major isomer), 3.62–3.60 (1H, m, minor isomer), 3.58–3.49 (2H, m, minor isomer), 2.36 (1H, ddd,

J 13.8, 4.3 and 2.9, major isomer), 1.85–1.40 (11H, m, both isomers), 1.32 (3H, d, *J* 6.7, Me, major isomer), 1.30 (3H, d, *J* 6.6, Me, minor isomer) and 0.96 (6H, t, *J* 7.3, Me, both isomers); δ_C (67.8) 118.3 (C, major isomer), 78.6 (CH, major isomer), 75.7 (minor isomer), 48.8 (CH, major isomer), 46.3 (CH, minor isomer), 37.1 (CH, major isomer), 36.9 (CH_2, minor isomer), 36.8 (CH_2, major isomer), 36.6 (CH, minor isomer), 34.5 (CH_2, major isomer), 33.1 (CH_2, minor isomer), 32.2 (CH_2, minor isomer), 22.5 (Me, major isomer), 22.3 (CH_2, major isomer), 21.9 (Me, minor isomer) and 13.1 (Me, both isomers). The sample decomposed before a mass spectrum could be obtained.

Cyclisation of 2-methoxycarbonylaminooct-4-ene 35e. (*E*)-Homoallylic carbamate **35e** (0.05 g, 0.23 mmol) was reacted under the conditions described in the general procedure (K_2CO_3) for 1 h. The crude product was purified by cc (methanol–dichloromethane 5 : 95) to afford a mixture of isomers **46e** in a ratio of 2 : 1 (0.03 g, 48%), as a yellow oil. The isomer ratio was determined by integration of the –OMe peaks in the ^{1}H NMR spectrum of the mixture. Data for the mixture: R_f 0.23 (methanol–dichloromethane 5 : 95); δ_H (250) 4.52–4.48 (1H, m, major isomer), 4.46–3.98 (4H, m, both isomers), 3.92–3.86 (1H, m, minor isomer), 3.69 (3H, s, OMe, major isomer), 3.68 (3H, s, OMe, minor isomer), 2.80–2.71 (1H, m, major isomer), 2.31–2.11 (2H, minor isomer), 2.03–1.20 (9H, m, both isomers), 1.22 (3H, d, *J* 6.6, Me, minor isomer), 1.20 (3H, d, *J* 6.6, Me, major isomer), 0.95 (3H, t, *J* 7.3, major isomer) and 0.93 (3H, t, *J* 7.3, minor isomer).

Iodocyclisations with no base present: general procedure

To a stirred solution of the cyclisation precursor (1.0 mmol, 1 eq.) in acetonitrile (1 ml) was added portionwise iodine (3.0 mmol, 3 eq.) and the reaction stirred at ambient temperature until complete according to TLC analysis (typically 2–20 min). TLC samples were taken every 30 seconds. The acetonitrile was removed under reduced pressure and the residue partitioned between dichloromethane (1 ml) and saturated aqueous sodium thiosulfate (1 ml). The resulting two layers were separated, and the aqueous layer extracted with dichloromethane (3 × 2 ml). The combined organic solutions were dried and evaporated to give crude products which were purified by column chromatography.

(2*SR*,3*RS*)-2-Ethyl-3-iodo-1-(*p*-tolylsulfonyl)pyrrolidine 36b. Homoallylic tosylamide **24b** (0.20 g, 0.80 mmol) was cyclised under the general conditions with no base and the reaction was complete within 2 min. The crude product was purified by cc (dichloromethane) followed by recrystallisation (hexane–ethyl acetate 9 : 1) to afford the *title compound* **36b** (0.27 g, 88%) as a colourless crystalline solid, mp 108–109 °C; other spectral and analytical data were identical to those displayed by samples prepared using either sodium hydrogen carbonate or potassium carbonate as the base (see above).

(2*RS*,3*SR*,5*SR*)-2-Butyl-3-iodo-5-methyl-1-(*p*-tolylsulfonyl)-pyrrolidine 37d. (*E*)-Homoallylic tosylamide **24d** (0.2 g, 0.7 mmol) was cyclised under the general conditions (no base), and the reaction was complete after 3 min. The crude product was purified by cc (dichloromethane) then recrystallised (hexane–ethyl acetate 9 : 1) to afford the *pyrrolidine* **37d** (0.25 g, 86%) as a colourless, crystalline solid mp 102–103 °C: R_f 0.56 (dichloromethane): ν_{max}/cm^{-1}($CHCl_3$) 2959 (s), 2924 (s), 2875 (w) and 1342 (s); δ_H (270) 7.77 (2H, d, *J* 8.3, Ar-H), 7.33 (2H, d, *J* 8.3, Ar-H), 4.09 (1H, ddd, *J* 5.7, 3.4 and 3.2, 3-H), 4.01–3.97 (1H, m, 2-H), 3.93 (1H, dqd, *J* 7.5, 6.6 and 6.2, 5-H), 2.43 (2H, s, Ar-Me), 2.20 (1H, ddd, *J* 13.9, 7.5 and 5.7, 4-H_α), 2.15 (1H, ddd, *J* 13.9, 6.2 and 3.4, 4-H_β), 1.43 (3H, d, *J* 6.6, 5-Me), 2.08–1.09 (6H, m, 1′-, 2′- and 3′-CH_2) and 0.92 (3H, t, *J* 7.3, 4′-Me); δ_C (67.8) 143.2, 134.2 (both Ar-C), 129.7, 128.1 (both Ar-CH), 72.9 (2-CH), 56.4 (5-CH), 45.0 (4-CH_2), 37.5 (1′-CH_2), 28.0 (2′-CH_2), 22.6 (3′-CH_2), 22.2 (Ar-Me), 22.1 (3-CH), 21.6 (5-Me) and 14.0 (4′-Me); *m/z* (FAB) 422 (M^+ + 1, 100%), 410 (11), 364 (52), 335 (20), 294 (55), 237 (23), 198 (81), 154 (74), 136 (64), 91 (75) and 77 (29) [Found: C, 45.7; H, 6.0; N, 3.5; M^+ + 1, 422.0682. $C_{16}H_{24}INO_2S$ requires C, 45.6; H, 5.7; N, 3.3%, $C_{16}H_{25}INO_2S$ requires *M*, 422.0652].

(2*S*,3*R*,5*R*)-2-Butyl-3-iodo-5-methyl-1-(*p*-tolylsulfonyl)-pyrrolidine 37e. (2*R*)-(*E*)-Homoallylic tosylamide **24e** (20 mg, 0.07 mmol) in acetonitrile (0.2 ml) was cyclised under the conditions described in the general procedure (no base) to give a yellow oil which was purified by recrystallisation (hexane–ethyl acetate 9 : 1) to afford the *iodopyrrolidine* **37e** (25 mg, 85%) as a colourless, crystalline solid, mp 112–114 °C: $[\alpha]_D$ + 14.0 (*c* 0.015 in $CHCl_3$); other spectral and analytical data, except the melting point, were identical to those obtained for the racemic product **37d** (see above).

(2*RS*,3*SR*,5*SR*)-2-Butyl-5-ethyl-3-iodo-1-(*p*-tolylsulfonyl)-pyrrolidine 37f. *i) By iodocyclisation of sulfonamide **24f**.* (*E*)-Homoallylic tosylamide **24f** (0.20 g, 0.64 mmol) was cyclised under the general conditions described above (no base); the reaction was complete after 3 min. The crude product was purified by cc (dichloromethane) then recrystallised (ethyl acetate–hexane 15 : 85) to give the *iodopyrrolidine* **37f** (0.23 g, 78%) as a pale orange, crystalline solid: mp 94–95 °C; R_f 0.56 (dichloromethane); ν_{max}/cm^{-1}($CHCl_3$) 2918 (s), 2930 (s), 2889 (s), 1597 (w), 1335 (s) and 1304 (s); δ_H (250) 7.77 (2H, d, *J* 8.2, Ar-H), 7.34 (2H, d, *J* 8.2, Ar-H), 4.07 (1H, ddd, *J* 5.6, 3.5 and 3.4, 3-H), 3.95 (1H, ddd, *J* 9.1, 3.6 and 3.4, 2-H), 3.72 (1H, dddd, *J* 8.0, 7.5, 6.8 and 4.2, 5-H), 2.43 (3H, s, Ar-Me), 2.10 (1H, ddd, *J* 14.2, 7.5 and 5.6, 4-H_α), 2.02 (1H, ddd, *J* 14.2, 6.8 and 3.5, 4-H_β), 1.77 (1H, ddq, *J* 13.3, 8.0 and 7.2, 1″-H_α), 1.44 (1H, dqd, *J* 13.3, 7.2 and 4.2, 1″-H_β), 1.41–1.28 (6H, m, 1′- 2′- and 3′-CH_2), 0.92 (3H, t. *J* 7.2, Me) and 0.90 (3H, t, *J* 7.2, Me); δ_C (100) 141.4, 136.3 (both Ar-C), 129.4, 127.9, (both Ar-CH), 72.7 (2-CH), 61.9 (5-CH), 41.9 (4-CH_2), 37.1 (1′-CH_2), 28.4 (1″-CH_2), 24.5, 22.5 (both CH_2), 22.3 (Ar-Me), 21.9 (3-CH), 14.0 (4′-Me) and 9.9 (2″-Me); *m/z* (FAB) 435 (M^+, 1%), 406 (19), 378 (80), 326 (7), 251 (47), 212 (48), 187 (7) and 91 (100) [Found: C, 47.3; H, 6.2; N, 3.2; M^+, 435.0745. $C_{17}H_{26}INSO_2$ requires C, 46.9; H, 6.0; N, 3.3%; *M*, 435.0729].

*ii) By acid-catalysed isomerisation of iodopyrrolidine **36f**.* The (2*SR*,3*RS*,5*SR*)-iodopyrrolidine **36f** (0.02 g, 0.05 mmol) in dry acetonitrile (0.2 ml) was treated with 57% aqueous hydrogen iodide (2 μl) and the mixture stirred at ambient temperature for 20 min. The standard sodium thiosulfate work-up described above afforded the *2,5-cis-pyrrolidine* **37f** (0.02 g, 94%) as a colourless solid, mp 95–97 °C (mixed mp 94–96 °C); other spectral and analytical data were identical to those displayed by the sample prepared by the iodocyclisation conditions described immediately above.

(2*SR*,3*RS*,5*SR*)-2-Butyl-5-ethyl-3-iodo-1-methylsulfonyl-pyrrolidine 36g. (*E*)-Homoallylic methanesulfonamide **24g** (0.01 g, 0.04 mmol) was cyclised under the conditions described in the general procedure (no base) and the reaction was complete after 3 min. The reaction was left for a further 30 min in an attempt to effect isomerisation. The crude product was purified by cc (dichloromethane) to afford the *title compound* **36g** (0.01 g, 78%) as a viscous, pale yellow oil: spectral and analytical data were identical to those obtained for the same substrate, cyclised in the presence of potassium carbonate.

(2*RS*,3*SR*,5*SR*)-5-Ethyl-3-iodo-2-pentyl-1-(*p*-tolylsulfonyl)-pyrrolidine 37h. (*E*)-Homoallylic tosylamide **24h** (0.05 g, 0.16 mmol) was cyclised under the general conditions described above (no base); the reaction was complete after 3 min. The

crude product was purified by cc (dichloromethane) to afford the *title compound* **37h** (0.05 g, 74%) as a pale orange, viscous oil: R_f 0.56 (dichloromethane); ν_{max}/cm^{-1} 2919 (s), 2930 (s), 2886 (s), 1711 (w), 1595 (w), 1337 (s) and 1301 (s); δ_H (250) 7.75 (2H, d, *J* 8.2, Ar-H), 7.33 (2H, d, *J* 8.2, Ar-H), 4.05 (1H, ddd, *J* 5.7, 3.5 and 3.4, 3-H), 3.94 (1H, ddd, *J* 9.1, 3.6 and 3.4, 2-H), 3.72 (1H, dddd, *J* 8.0, 7.5, 6.8 and 4.2, 5-H), 2.44 (3H, s, Ar-Me), 2.10 (1H, ddd, *J* 14.2, 7.5 and 5.7, 4-H_α), 2.02 (1H, ddd, *J* 14.2, 6.8 and 3.5, 4-H_β), 1.77 (1H, ddq, *J* 13.4, 8.0 and 7.1, 1″-H_α), 1.44 (1H, dqd, *J* 13.4, 7.1 and 4.2, 1″-H_β), 1.43–1.20 (8H, m, 1′-, 2′-, 3′- and 4′-CH_2), 0.92 (3H, t, *J* 7.3, Me) and 0.90 (3H, t, *J* 7.1, Me); δ_C (100) 141.2, 136.2 (both Ar-C), 129.4, 127.9, (both Ar-CH), 72.5 (2-CH), 61.9 (5-CH), 41.9 (4-CH_2), 37.1 (1′-CH_2), 28.4 (1″-CH_2), 22.5 (CH_2), 22.3 (Ar-Me), 22.1 (CH_2), 21.8 (3-CH), 14.2 (5′-Me) and 9.93 (2″-Me) [Found: C, 48.6; H, 6.4; N, 3.0. $C_{18}H_{28}INO_2S$ requires C, 48.1; H, 6.2; N, 3.1%].

(2*RS*,3*SR*,5*SR*)-5-Butyl-3-iodo-2-pentyl-1-(*p*-tolylsulfonyl)-pyrrolidine 37i. (*E*)-Homoallylic tosylamide **24i** (0.30 g, 0.85 mmol) was subjected to the general iodocyclisation conditions (no base), and the reaction was complete after 15 min. The crude product was purified by cc (dichloromethane) to yield the *iodopyrrolidine* **37i** (0.32 g, 76%) as a pale yellow, viscous oil: R_f 0.64 (dichloromethane); ν_{max}/cm^{-1} 2955 (s), 2928 (s), 2858 (w), 1685 (w), 1598 (w), 1455 (s) and 1346 (s); δ_H (250) 7.75 (2H, d, *J* 8.3, Ar-H), 7.33 (2H, d, *J* 8.3, Ar-H), 4.05 (1H, ddd, *J* 5.1, 3.4 and 3.3, 3-H), 3.94 (1H, ddd, *J* 8.7, 3.7 and 3.3, 2-H), 3.75 (1H, dddd, *J* 8.5, 7.8, 6.9 and 4.5, 5-H), 2.43 (3H, s, Ar-Me), 2.13–1.74 (4H, m, 1′- and 4-CH_2), 1.53–1.20 (12H, m, 1″-, 2′-, 2″-, 3′-, 3″ and 4′-CH_2), 0.94 (3H, t, *J* 7.2, Me) and 0.88 (3H, t, *J* 7.3, Me); δ_C (100) 143.5, 134.4 (both Ar-C), 129.6, 128.0 (both Ar-CH), 72.2 (2-CH), 60.6 (5-CH), 42.7 (4-CH_2), 37.1 (1′-CH_2), 35.3, 31.6, 27.9, 25.4, 22.5, 22.4 (all CH_2), 21.7 (3-CH), 21.5 (Ar-Me), 14.0 (Me) and 13.9 (Me); *m*/*z* (ES) 478 ($M^+ + 1$, 45%), 419 (100), 391 (24), 352 (33), 254 (56), 83 (28) and 60 (22) [Found: $M^+ + 1$, 478.1277. $C_{20}H_{33}INO_2S$ requires *M*, 478.1279] [Found: C, 50.3; H, 6.9; N, 3.1. $C_{20}H_{32}INO_2S$ requires C, 50.3; H, 6.8; N, 2.9%].

(2*RS*,3*SR*,5*SR*)-5-Ethyl-3-iodo-2-phenyl-1-(*p*-tolylsulfonyl)-pyrrolidine 37j. (*E*)-Homoallylic tosylamide **24j** (0.50 g, 1.52 mmol) was cyclised under the foregoing general conditions (no base), and the reaction was complete after 10 min. The crude product was purified by cc (dichloromethane) followed by recrystallisation (hexane–ethyl acetate 9 : 1) to yield the *iodopyrrolidine* **37j** (0.42 g, 76%) as a colourless, flaky solid: mp 110–112 °C; R_f 0.54 (dichloromethane); $\nu_{max}/cm^{-1}(CHCl_3)$ 3061 (w), 2966 (s), 2993 (s), 2876 (w), 1446 (w) and 1349 (s); δ_H (400) 7.96 (2H, d, *J* 8.3, Ar-H), 7.42–7.25 (7H, m, Ar-H), 4.98 (1H, d, *J* 4.9, 2-H), 4.11 (1H, ddd, *J* 6.2, 6.2 and 4.9, 3-H), 3.92 (1H, dddd, *J* 9.6, 6.2, 6.2 and 4.5, 5-H), 2.43 (3H, s, Ar-Me), 2.28 (1H, ddq, *J* 13.5, 9.6 and 7.5, 1′-H_α), 2.12 (2H, app. dd, *J* 6.2 and 6.2, 4-CH_2), 1.75 (1H, dqd, *J* 13.5, 7.5 and 4.5, 1′-H_β) and 1.01 (3H, t, *J* 7.5, 2′-Me); δ_C (100) 142.8, 140.1, 139.3 (all Ar-C), 129.1, 128.5, 127.8, 127.1, 126.4 (all Ar-CH), 76.6 (2-CH), 63.6 (5-CH), 38.4 (4-CH_2), 26.8 (1′-CH_2), 24.7 (3-CH), 21.5 (Ar-Me) and 11.1 (2′-Me); *m*/*z* (ES) 456 ($M^+ + 1$, 54%), 330 (6), 276 (15), 106 (100) and 74 (17) [Found: C, 50.4; H, 5.1; N, 3.2. $C_{19}H_{22}INO_2S$ requires C, 50.1; H, 4.9; N, 3.1%].

(2*RS*,3*SR*,5*SR*)-1-Phenylsulfonyl-5-ethyl-3-iodo-2-phenyl-pyrrolidine 37k. The (*E*)-homoallylic benzenesulfonamide **24k** (0.677 g, 2.15 mmol) was cyclised under the foregoing general conditions (no base); the reaction was complete after 10 min. The crude product was purified by cc (dichloromethane) followed by recrystallisation from hexane–ethyl acetate (8 : 1) to give the *iodopyrrolidine* **37k** (0.768 g, 81%) as orange clusters: mp 102–104 °C (see discussion); R_f 0.51 (dichloromethane); ν_{max}/cm^{-1} ($CHCl_3$) 3061 (w), 2966 (s), 2930 (s), 2876 (w), 1446 (w) and 1349 (s); δ_H 7.85–7.31 (10H, m, 2 × Ph), 5.01 (1H, d, *J* 5.0, 2-H), 4.13 (1H, ddd, *J* 6.2, 6.2 and 5.0, 3-H), 3.94 (1H, dddd, *J* 9.8, 6.2, 6.2 and 4.4, 5-H), 2.30 (1H, ddq, *J* 13.3, 9.8 and 7.5, 1′-H_α), 2.14–2.07 (2H, m, 4-CH_2), 1.75 (1H, dqd, *J* 13.3, 7.3 and 4.4, 1′-H_β) and 0.98 (3H, t, *J* 7.3, 2′-Me); δ_C 140.8, 137.8, (both Ph-C), 132.9, 128.9, 128.5, 127.9, 126.5 (all Ph-CH), 74.8 (2-CH), 62.8 (5-CH), 41.7 (4-CH_2), 28.7 (1′-CH_2), 26.0 (3-CH) and 10.7 (2′-Me); *m*/*z* (FAB) 442 ($M^+ + 1$, 19%), 410 (53), 380 (46), 252 (63), 184 (66), 133 (100) and 77 (49) [Found: C, 49.2; H, 4.6; N, 3.2. $C_{18}H_{20}INO_2S$ requires C, 49.0; H, 4.6; N, 3.2%].

(2*SR*,3*RS*,4*SR*,5*RS*)-4,5-Dimethyl-3-iodo-2-propyl-1-(*p*-tolylsulfonyl)pyrrolidine 38. (*E*)-Homoallylic tosylamide **27b** (0.10 g, 0.34 mmol) was cyclised under the general conditions (no base), and the reaction was complete after 5 min. The reaction was stirred at ambient temperature for a further 30 min to effect possible isomerisation. The crude product was purified by cc (dichloromethane) followed by recrystallisation (hexane–ethyl acetate 9 : 1) to afford the *title compound* **38** (0.12 g, 82%) as a colourless solid, mp 103–104 °C: the spectral and analytical data were identical to those obtained for the same substrate when cyclised in the presence of potassium carbonate.

(2*SR*,3*RS*,4*SR*,5*SR*)-4,5-Dimethyl-3-iodo-2-propyl-1-(*p*-tolylsulfonyl)pyrrolidine 39. (*E*)-Homoallylic tosylamide **28b** (0.10 g, 0.34 mmol) was cyclised under the general conditions (no base), and the reaction was complete after 4 min. The reaction was stirred at ambient temperature for a further 30 min to effect possible isomerisation. The crude product was purified by cc (dichloromethane) followed by recrystallisation (hexane–ethyl acetate 9 : 1) to yield the *title compound* **39** (0.11 g, 78%) as a solid, mp 110–111 °C. The spectral and analytical data were identical to those obtained from the potassium carbonate reaction described previously.

Cyclisation of (*Z*)-3-(*p*-tolylsulfonylamino)dec-5-ene 26c. The (*Z*)-homoallylic tosylamide **26c** (0.05 g, 0.16 mmol) was reacted under the conditions described in the general procedure (no base) for 1 h. Purification by cc (dichloromethane) afforded an unresolvable mixture of isomers in the ratio 4 : 1 : 1 (0.04 g, 57%). The two minor isomers were found (by comparison of the ^{1}H NMR spectrum of the mixture) to be the (2*SR*,3*RS*,5*SR*)-pyrrolidine **36f** and the (2*RS*,3*SR*,5*SR*)-pyrrolidine **37f** obtained from the cyclisation of the corresponding (*E*)-precursor **24f** under acidic and basic conditions, respectively. The ^{1}H and ^{13}C NMR spectra were sufficiently well resolved to assign the peaks for the major isomer: R_f 0.52 (dichloromethane); $\nu_{max}/cm^{-1}(CHCl_3)$ 2948 (s), 2930 (s), 2868 (w), 1475 (w) and 1340 (s); δ_H (400) 7.69 (2H, d, *J* 8.3, Ar-H), 7.31 (2H, d, *J* 8.3, Ar-H), 3.80 (1H, ddd, *J* 9.8, 6.6 and 3.8, 3-H), 3.51–3.44 (1H, m, 5-H), 3.27 (1H, ddd, *J* 12.5, 7.0 and 6.6, 2-H), 2.45 (3H, s, Ar-Me), 2.12–1.92 (4H, m), 1.45–1.28 (6H, m), 0.93 (3H, t, *J* 7.4, Me) and 0.90 (3H, t, *J* 7.3, Me); δ_C (67.8) 142.8, 135.6 (both Ar-C), 129.9, 127.5 (both Ar-CH), 63.6, 62.3 (both CH), 41.4, 33.6, 31.0, 28.4, 22.5 (all CH_2), 21.5 (Ar-Me), 20.9 (3-CH), 14.0 (4″-Me) and 10.2 (2″-Me); *m*/*z* (FAB), 436 ($M^+ + 1$, 100%), 308 (95), 212 (84), 155 (69), 91 (86), 68 (49) and 56 (52) [Found: $M^+ + 1$, 436.0770. $C_{17}H_{27}INO_2S$ requires *M*, 436.0807], which was tentatively assigned the all-*cis* structure **44**.

(2*SR*,3*RS*,3a*SR*,7a*RS*)-2-Butyl-3-iodo-1-(*p*-tolylsulfonyl)-octahydroindole 40. (*E*)-Tosylamide **31** (20 mg, 0.06 mmol) was cyclised under the conditions described in the general procedure (no base), and the reaction was complete after 15 min. The crude product was purified by cc (hexane–ether 4 : 1) to afford the *title compound* **40** (20 mg, 75%) as a yellow oil: ν_{max}/cm^{-1} 2952 (s), 2935 (s), 2884 (s), 1342 (s) and 1294 (s); δ_H (400) 7.73 (2H, d, *J* 8.1, Ar-H), 7.33 (2H, d, *J* 8.1, Ar-H), 3.96 (1H, dd, *J* 11.7 and 8.6, 3-H), 3.92–3.87 (1H, m, 2-H), 3.57 (1H, dt, *J* 11.2 and 6.8, 7a-H), 2.45 (3H, s, Ar-Me), 2.02–0.98 (15H, m)

and 0.95 (3H, t, *J* 7.2, Me); δ_C (100) 143.6, 134.8 (both Ar-C), 129.8, 127.4 (both Ar-CH), 69.6, 59.7 (both CH), 47.3 (3a-CH), 33.9, 30.8 (both CH_2), 27.2 (CHI), 26.9, 24.6, 24.4, 22.8 (all CH_2), 21.6 (Ar-Me), 20.1 (CH_2) and 14.0 (Me); *m*/*z* (ES) 462 ($M^+ + 1$, 5%), 336 (15), 124 (71) and 58 (100) [Found: $M^+ + 1$, 462.0964. $C_{19}H_{29}INO_2S$ requires *M*, 462.0967].

(2*RS*,3*RS*,3a*SR*,7a*RS*)-2-Butyl-3-iodo-1-(*p*-tolylsulfonyl)-octahydroindole 41. (*Z*)-Tosylamide **32** (12 mg, 0.03 mmol) was cyclised under the conditions described in the general procedure (no base), and the reaction was complete after 3 h. The crude product was purified by cc (hexane–ether 80 : 20) to afford the *title compound* **41** (7 mg, 43%) as a yellow oil: ν_{max}/cm^{-1} 2950 (s), 2937 (s), 2879 (s), 1350 (s) and 1300 (s); δ_H (400) 7.74 (2H, d, *J* 8.3, Ar-H), 7.29 (2H, d, *J* 8.3, Ar-H), 4.45 (1H, dd, *J* 12.7 and 7.8, 3-H), 3.90–3.83 (2H, m, 2- and 7a-H), 2.43 (3H, s, Ar-Me), 2.27–2.20 (1H, m), 2.01–1.87 (2H, m), 1.64–1.08 (12H, m) and 0.83 (3H, t, *J* 7.2, Me); δ_C (100) 143.4, 133.2 (both Ar-C), 129.5, 127.2 (both Ar-CH), 60.4, 59.7 (both CH), 44.2 (3a-CH), 35.8 (CH_2), 30.9 (CHI), 28.8, 28.0, 25.4, 23.8, 22.7 (all CH_2), 21.4 (Ar-Me), 19.7 (CH_2) and 14.0 (Me); *m*/*z* (ES) 462 ($M^+ + 1$, 3%), 124 (42) and 58 (100) [Found: $M^+ + 1$, 462.0964].

Cyclisation of (*E*)-2-(*N*-*tert*-butoxycarbonylamino)oct-4-ene 35a. (*E*)-Homoallylic amide **35a** (0.03 g, 0.13 mmol) was cyclised under the conditions described in the general procedure (no base) for 30 min. The crude product was purified by cc (methanol–dichloromethane 5 : 95) to afford the homoallylic amine **35b** (0.002 g, 15%) as a yellow oil (spectral and analytical data were identical to the sample prepared earlier), and the carbamates as a mixture of isomers **45** in the ratio 2 : 1 (0.03 g, 67%) as a viscous yellow oil: spectral and analytical data were identical to those from the product of the same substrate with potassium carbonate as the base.

Cyclisation of (*E*)-2-acetylaminooct-4-ene 35d. (*E*)-Homoallylic amide **35d** (0.10 g, 0.4 mmol) in acetonitrile (2 ml) was reacted under the conditions described in the general procedure (no base) for 1 h. The crude product was purified by cc (dichloromethane) to afford a mixture of isomers **46d** in the ratio 2 : 1 (0.07 g, 67%) as a yellow oil. The isomer ratio was determined by measurement of acetyl-methyl peaks from the ^{1}H NMR spectrum. Data for the mixture: R_f 0.49 (dichloromethane); ν_{max}/cm^{-1} 2948 (s), 2929 (s), 1691, 1419 (s) and 1341 (s); δ_H (250) 4.59–4.41 (4H, m, both isomers), 4.25–4.12 (2H, m, both isomers), 2.67 (3H, s, Me, minor isomer), 2.64 (3H, s, Me, major isomer), 2.04–1.40 (12 H, m, both isomers), 1.68 (3H, d, *J* 6.6, Me, minor isomer), 1.62 (3H, d, *J* 6.6, Me, major isomer), 1.02 (3H, t, *J* 7.3, Me, minor isomer) and 1.01 (3H, t, *J* 7.3, major isomer); δ_C (100, major isomer only) 83.2, 48.1, 37.0, 34.6, 32.7, 23.0, 21.8, 19.6 and 13.4.

Cyclisation of (*E*)-2-methoxycarbonylaminooct-4-ene 35e. (*E*)-Homoallylic sulfonamide **35e** (0.05 g, 0.23 mmol) was reacted under the conditions described in the general procedure (no base) for 1 h. The crude product was purified by cc (dichloromethane) to afford a mixture of isomers in the ratio 2 : 1 (0.03 g, 42%) as a yellow oil. The ratio of isomers and **46e** was determined by measurement of the OME resonances in the ^{1}H NMR spectrum. The two isomers were identical to those obtained from the same substrate when potassium carbonate was used as the base.

Deiodination of iodopyrrolidines: general procedure

To a stirred solution of a 3-iodopyrrolidine (1 mmol, 1 eq.) in dry, degassed toluene (50 ml) under nitrogen was added tributyltin hydride (2.91 g, 10 mmol) and the reaction mixture heated at reflux until complete reduction according to TLC analysis (typically 2–5 h). The reaction mixture was cooled and the toluene evaporated. The remaining crude product was dissolved in acetonitrile (10 ml) and extracted with hexane (3 × 10 ml) to remove any organotin residues. The acetonitrile was evaporated to yield the required product which was purified by column chromatography.

(2*SR*,5*SR*)-2-Butyl-5-methyl-1-(*p*-tolylsulfonyl)pyrrolidine 49a. Iodopyrrolidine **36d** (0.05 g, 0.12 mmol) was deiodinated as described above to give the *title compound* **49a** (0.03g, 88%) as a colourless, viscous oil: R_f 0.32 (dichloromethane); ν_{max}/cm^{-1} 2959 (s), 2938 (s), 2875 (w) and 1355 (s); δ_H (250) 7.73 (2H, d, *J* 8.3, Ar-H), 7.25 (2H, d, *J* 8.3, Ar-H), 4.02 (1H, dqd, *J* 6.5, 6.3 and 1.2, 5-H), 3.84–3.77 (1H, m, 2-H), 2.41 (3H, s, Ar-Me), 2.08–1.09 (10H, m, 1-, 2-, 3′-, 3′- and 4′-CH_2), 1.19 (3H, d, *J* 6.3, 1″-Me) and 0.85 (3H, t, *J* 7.2, 4′-Me); δ_C (100) 142.4, 139.3 (both Ar-C), 129.3, 126.9 (both Ar-CH), 60.7 (5-CH), 56.3 (2-CH), 33.9 (1′-CH_2), 31.5, 28.5, 27.7, 22.5 (all CH_2), 21.4 (Ar-Me), 21.1 (1″-Me) and 14.0 (4′-Me); *m*/*z* (ES) 296 ($M^+ + 1$, 100%), 125 (3), 102 (4) and 60 (7) [Found: $M^+ + 1$, 296.1680. $C_{16}H_{26}NO_2S$ requires *M*, 296.1684].

(2*SR*,5*SR*)-2-Butyl-5-ethyl-1-(*p*-tolylsulfonyl)pyrrolidine 49b. 3-Iodopyrrolidine **36f** (0.05 g, 0.12 mmol) was deiodinated as described above to give the *title compound* **49b** (0.03 g, 84%) as a colourless, viscous oil: R_f 0.32 (dichloromethane); ν_{max}/cm^{-1} 2959 (s), 2940 (s), 2877 (s) and 1355 (s); δ_H (250) 7.71 (2H, d, *J* 8.2, Ar-H), 7.23 (2H, d *J* 8.2, Ar-H), 3.84–3.70 (2H, m, 2- and 5-H), 2.40 (3H, s, Ar-Me), 2.03–1.05 (12H, m, 1-, 2-, 3′, 3′- and 4′-CH_2), 0.93 (3H, t, *J* 7.3, Me) and 0.90 (3H, t, *J* 6.9, Me); δ_C (100) 142.1, 139.8 (both Ar-C), 129.0, 126.6 (both Ar-CH), 62.4 (5-CH), 56.3 (2-CH), 33.8, 31.9, 28.3, 27.4, 26.4, 22.3 (all CH_2), 21.3 (Ar-Me), 13.9 (4′-Me) and 10.7 (2″-Me); *m*/*z* (ES) 310 ($M^+ + 1$, 100%), 281 (35) and 91 (20) [Found: $M^+ + 1$, 310.1837. $C_{17}H_{28}NO_2S$ requires *M*, 310.1841].

(2*SR*,5*SR*)-5-Ethyl-2-pentyl-1-(*p*-tolylsulfonyl)pyrrolidine 49c. 3-Iodopyrrolidine **36h** (0.05 g, 0.11 mmol) was deiodinated as described above to give the *title compound* **49c** (0.03 g, 84%) as a colourless, viscous oil: R_f 0.34 (dichloromethane); ν_{max}/cm^{-1} 2958 (s), 2940 (s), 2875 (s) and 1357 (s); δ_H (250) 7.72 (2H, d, *J* 8.2, Ar-H), 7.25 (2H, d, *J* 8.2, Ar-H), 3.87–3.71 (2H, m, 2- and 5-H), 2.41 (3H, s, Ar-Me), 2.03–1.02 (14H, m, 1′-, 1″-, 2′-, 3-, 3′-, 4- and 4′-CH_2), 0.92 (3H, t, *J* 7.3, Me) and 0.89 (3H, t, *J* 6.9, Me); δ_C (100) 142.2, 139.7 (both Ar-C), 129.3, 126.8 (both Ar-CH), 62.2 (5-CH), 56.3 (2-CH), 33.8, 31.6, 27.9, 27.4, 26.7, 26.1, 22.5 (all CH_2), 21.4 (Ar-Me), 14.0 (5′-Me) and 10.64 (2″-Me); *m*/*z* (FAB) 324 ($M^+ + 1$, 10%), 291 (19), 235 (44), 179 (100) and 91 (9) [Found: $M^+ + 1$, 324.1985. $C_{18}H_{30}NO_2S$ requires *M* 324.1997].

(2*SR*,5*SR*)-5-Butyl-2-pentyl-1-(*p*-tolylsulfonyl)pyrrolidine 49d. Iodopyrrolidine **36i** (0.07 g, 0.15 mmol) was deiodinated as described above to yield the *title compound* **49d** (0.04 g, 82%) as a colourless, viscous oil: R_f 0.48 (dichloromethane); ν_{max}/cm^{-1} 2959 (s), 2936 (s), 2872 (w), 1464 (w) and 1355 (s); δ_H (250) 7.72 (2H, d, *J* 8.3, Ar-H), 7.26 (2H, d, *J* 8.3, Ar-H), 3.81 (2H, m, 2- and 5-H), 2.42 (3H, s, Ar-Me), 1.92–1.13 (18H, 1′-, 1″-, 2′-, 2″-, 3′-, 3″-, 4- and 4′-CH_2), 0.88 (3H, t, *J* 7.3, Me) and 0.85 (3H, t, *J* 7.1, Me); δ_C (100) 142.4, 140.1 (both Ar-C), 129.3, 126.9 (both Ar-CH), 60.9 (2-CH and 5-CH), 33.8, 33.6, 31.6, 31.1, 28.6, 28.0, 26.1, 22.6 (all CH_2), 21.4 (Ar-Me) and 14.0 (4″- and 5′-Me); *m*/*z* (ES) 352 ($M^+ + 1$, 100%), 296 (13), 291 (18), 235 (20), 102 (14) and 83 (17) [Found: $M^+ + 1$, 352.2310. $C_{20}H_{34}NO_2S$ requires 352.2312].

(2*RS*,5*SR*)-5-Ethyl-2-phenyl-1-(*p*-tolylsulfonyl)pyrrolidine 49e. Iodopyrrolidine **36j** (0.20 g, 0.60 mmol) was deiodinated as described above to yield the *title compound* **49e** (0.16 g, 82%) as a viscous, colourless oil; R_f 0.34 (dichloromethane); ν_{max}/cm^{-1}

2959 (s), 2945 (s), 2875 (w), 1461 (w) and 1349 (s); δ_H (250) 7.37 (2H, d, *J* 8.3, Ar-H), 7.17–7.00 (7H, m, Ar-H), 5.98 (1H, dd, *J* 7.9 and 1.4, 2-H), 4.07–4.04 (1H, m, 5-H), 2.43–2.39 (1H, m, 3-H_α), 2.35 (3H, s, Ar-Me), 2.25–2.09 (2H, m, 4- and 1′-H_α), 1.82–1.67 (2H, m, 3- and 4-H_β), 1.51 (1H, dqd, *J* 13.4, 7.4 and 2.9, 1′-H_β) and 0.90 (3H, t, *J* 7.4, 2′-Me); δ_C (100) 142.5, 142.2, 138.9 (all Ar-C), 128.8, 127.9, 126.8, 126.8, 126.5 (all Ar-CH), 63.9 (2-CH), 63.0 (5-CH), 33.3 (1′-CH_2), 27.4 (3-CH_2), 27.2 (4-CH_2), 21.3 (Ar-Me) and 10.6 (1′-Me); *m/z* (ES) 330 (M^+ + 1, 100%), 176 (27), 174 (38), 102 (8), 85 (8) and 60 (19) [Found: M^+ + 1, 330.1529 $C_{19}H_{24}NO_2S$ requires 330.1532].

(2*RS*,5*SR*)-2-Butyl-5-methyl-1-(*p*-tolylsulfonyl)pyrrolidine 50a. Iodopyrrolidine **37d** (0.05 g, 0.12 mmol) was deiodinated under the conditions described in the general procedure to afford the *title compound* **50a** (0.03 g, 86%) as a colourless, viscous oil: R_f 0.32 (dichloromethane); ν_{max}/cm^{-1} 2960 (s), 2942 (s), 2875 (w) and 1357 (s); δ_H (400) 7.71 (2H, d, *J* 8.1, Ar-H), 7.29 (2H, d, *J* 8.1, Ar-H), 3.69–3.63 (1H, m, 5-H), 3.58–3.53 (1H, m, 2-H), 2.42 (3H, s, Ar-Me), 1.89–1.27 (10H, m, 1′-, 2′- 3-, 3′- and 4′-CH_2), 1.32 (3H, d, *J* 6.3, 1″-Me) and 0.92 (3H, t, *J* 7.2, 4′-Me); δ_C (100) 143.4, 143.2 (both Ar-C), 129.5, 127.4 (both Ar-CH), 61.9 (5-CH), 57.2 (2-CH), 36.9, 32.1, 29.5, 28.4 (all CH_2), 23.5 (1″-Me), 22.6 (CH_2), 21.4 (Ar-Me) and 14.0 (4′-Me); *m/z* (ES) 296 (M^+ + 1, 100%), 276 (6) and 221 (5) [Found: M^+ + 1, 296.1677].

(2*RS*,5*SR*)-2-Butyl-5-ethyl-1-(*p*-tolylsulfonyl)pyrrolidine 50b. Iodopyrrolidine **37f** (0.05 g, 0.12 mmol) was deiodinated under the conditions described in the general procedure to afford the *title compound* **50b** (0.03 g, 81%) as a colourless, viscous oil: R_f 0.35 (dichloromethane); ν_{max}/cm^{-1} 2960 (s), 2943 (s), 2874 (w) and 1355 (s); δ_H (400) 7.72 (2H, d, *J* 8.2, Ar-H), 7.32 (2H, d, *J* 8.2, Ar-H), 3.55–3.45 (1H, m, 2- and 5-H), 2.42 (3H, s, Ar-Me), 1.91–1.12 (12H, m, 1′-, 1″-, 2-, 3-, 3′- and 4′- CH_2), 0.92 (3H, t, *J* 7.3, Me) and 0.87 (3H, t, *J* 7.2, Me); δ_C (67.8) 142.8, 135.7 (both Ar-C), 129.5, 127.3 (both Ar-CH), 62.7, 61.4 (both CH), 37.2, 32.0, 29.8, 29.6, 25.8, 22.4 (all CH_2), 21.5 (Ar-Me), 13.8 (4′-Me) and 10.5 (2″-Me); *m/z* (ES) 310 (M^+ + 1, 100%), 281 (26), 125 (43), and 91 (23) [Found: M^+ + 1, 310.1836].

(2*RS*,5*SR*)-5-Ethyl-2-pentyl-1-(*p*-tolylsulfonyl)pyrrolidine 50c. Iodopyrrolidine **37h** (0.06 g, 0.11 mmol) was deiodinated by the general procedure to afford the *pyrrolidine* **50c** (0.03 g, 82%) as a colourless, viscous oil: R_f 0.34 (dichloromethane); ν_{max}/cm^{-1} 2959 (s), 2943 (s), 2872 (w) and 1356 (s); δ_H (400) 7.71 (2H, d, *J* 8.2, Ar-H), 7.30 (2H, d, *J* 8.2, Ar-H), 3.56–3.47 (2H, m, 2- and 5-H), 2.41 (3H, s, Ar-Me), 1.91–1.12 (14H, m, 1′-, 1″-, 2′-, 3-, 3′-, 4- and 4′-CH_2), 0.92 (3H, t, *J* 7.3, Me) and 0.88 (3H, t, *J* 7.2, Me); δ_C (67.8) 142.9, 135.4 (both Ar-C), 129.5, 127.4 (both Ar-CH), 62.9, 61.7 (both CH), 37.1, 31.7, 29.8, 29.5, 29.1, 25.9, 22.6 (all CH_2), 21.5 (Ar-Me), 14.0 (5′-Me) and 10.5 (2″-Me); *m/z* (FAB) 324 (M^+ + 1, 7%), 297 (22), 235 (43), 179 (100) and 91 (10) [Found: M^+ + 1, 324.1996].

(2*RS*,5*SR*)-5-Butyl-2-pentyl-1-(*p*-tolylsulfonyl)pyrrolidine 50d. Iodopyrrolidine **37i** (0.05 g, 0.11 mmol) was deiodinated as described in the general procedure to yield the *title compound* **50d** (0.03 g, 83%) as a colourless, viscous oil: R_f 0.50 (dichloromethane); ν_{max}/cm^{-1} 2959 (s), 2931 (s), 2861 (w), 1461 (w) and 1335 (s); δ_H (250) 7.71 (2H, d, *J* 8.3, Ar-H), 7.29 (2H, d, *J* 8.3, Ar-H), 3.56–3.48 (2H, m, 2- and 5-H), 1.88–1.09 (18H, m, 1′-, 1″-, 2′-, 2″-, 3-, 3′-, 3″-, 4- and 4′-CH_2), 0.94 (3H, t, *J* 7.2, Me) and 0.87 (3H, t, *J* 6.7, Me); δ_C (100) 142.8, 135.2 (both Ar-C), 129.5, 127.6 (both Ar-CH), 61.7 (2- and 5-CH), 37.2, 36.9, 31.7, 29.8, 29.6, 28.5, 25.9, 22.6, 22.6 (all CH_2), 21.5 (Ar-Me) and 14.1 (4″- and 5′-Me); *m/z* (ES) 352 (M^+ + 1, 100%), 291 (17), 235 (20), 102 (14) and 83 (15). These data are consistent with those in the literature.[41]

(2*SR*,5*SR*)-5-Ethyl-2-phenyl-1-(*p*-tolylsulfonyl)pyrrolidine 50e. Iodopyrrolidine **37j** (0.10 g, 0.30 mmol) was deiodinated as described above to yield the *title compound* **50e** (0.08 g, 85%) as a colourless, viscous oil: R_f 0.36 (dichloromethane); ν_{max}/cm^{-1} 2960 (s), 2942 (s), 2875 (w), 1461 (w) and 1349 (s); δ_H (250) 7.72 (2H, d, *J* 8.3, Ar-H), 7.41–7.21 (7H, m, Ar-H), 5.98 (1H, dd, *J* 6.9 and *J* 6.9, 2-H), 3.72 (1H, dddd, *J* 11.4, 7.4, 6.9 and 4.7, 5-H), 2.44 (3H, s, Ar-Me), 2.09 (1H, dqd, *J* 13.1, 7.3 and 4.7, 1′-H_α), 1.97–1.82 (2H, m, 3-CH_2), 1.66–1.53 (3H, m, 1′-H_β and 4-CH_2) and 0.99 (3H, t, *J* 7.4, 2′-Me); δ_C (100) 143.2, 142.8, 135.1 (all Ar-C), 129.5, 128.2, 127.6 (all Ar-CH), 126.9 (Ar-CH), 128.2 (Ar-CH), 64.6 (2-CH), 63.8 (5-CH), 34.2 (1′-CH_2), 29.5 (3-CH_2), 29.3 (4-CH_2), 21.4 (Ar-Me) and 10.9 (2′-Me); *m/z* (ES) 330 (M^+ + 1, 100%), 176 (23), 174 (63), 83 (7) and 60 (17) [Found: M^+ + 1, 330.1528. $C_{19}H_{24}NO_2S$ requires 330.1532].

Elimination of hydrogen iodide from iodopyrrolidines: general procedure

A solution of the 3-iodopyrrolidine (1.0 mmol, 1 eq.) and DBU (0.18 g, 1.2 mmol, 1.2 eq.) in toluene (10 ml) was heated at reflux until the reaction was complete according to the TLC analysis (typically 2–5 h). The reaction mixture was cooled, quenched with aqueous 2 M hydrochloric acid (5 ml) and the resulting two layers separated. The aqueous layer was extracted with ether (3 × 10 ml) and the combined organic solutions dried and the solvent evaporated to yield the product.

(2*RS*,5*SR*)-5-Ethyl-2-phenyl-1-(*p*-tolylsulfonyl)-3-pyrroline 51. Iodopyrrolidine **36j** (0.05 g, 0.11 mmol) was reacted as described above to give the *3-pyrroline* **51** (0.03 g, 78%) as a viscous, colourless oil: R_f 0.48 (dichloromethane); δ_H (270) 7.19–6.83 (9H, m, Ar-H), 5.69 (1H, ddd, *J* 6.3, 1.9 and 1.6, 3-H), 5.58 (1H, ddd, *J* 6.3, 2.0 and 1.8, 4-H), 5.50 (1H, ddd, *J* 5.3, 2.0 and 1.9, 2-H), 4.69–4.57 (1H, m, 5-H), 2.23 (3H, s, Ar-Me), 2.14–1.85 (2H, m, 1′-CH_2) and 0.88 (3H, t, *J* 7.2, 2′-Me); δ_C (67.8) 141.8, 138.1, 137.7 (all Ar-C), 129.9 (Ar-CH), 129.0 (3-CH), 128.9 (4-CH), 128.7, 127.9, 127.8, 126.4 (all Ar-CH), 71.6 (2-CH), 67.7 (5-CH), 28.4 (1′-CH_2), 21.2 (Ar-Me) and 8.0 (2′-Me); *m/z* (ES) 328 (M^+ + 1, 97%), 245 (7), 157 (8) and 102 (8) [Found: M^+ + 1, 328.1371. $C_{19}H_{22}NO_2S$ requires *M*, 328.1371].

(2*SR*,5*SR*)-5-Ethyl-2-phenyl-1-(*p*-tolylsulfonyl)-3-pyrroline 52. Iodopyrrolidine **37j** (0.05 g, 0.11 mmol) was reacted as described in the general procedure above to yield the *3-pyrroline* **52** (0.03 g, 72%) as a viscous, colourless oil: R_f 0.48 (dichloromethane); δ_H (270) 7.56 (2H, d, *J* 8.2, Ar-H), 7.32–7.15 (7H, m, Ar-H), 5.68 (1H, ddd, *J* 6.3, 2.0 and 1.9, 3-H), 5.56 (1H, ddd, *J* 6.3, 2.0 and 1.9, 4-H), 5.40 (1H, ddd, *J* 2.0, 2.0 and 2.0, 2-H), 4.46–4.38 (1H, m, 5-H), 2.33 (3H, s, Ar-Me), 1.99–1.53 (2H, m, 1′-CH_2) and 0.90 (3H, t, *J* 7.6, 2′-Me); δ_C (270) 143.8, 141.3, 135.7 (all Ar-C), 130.0, 129.7, 129.1, 128.8, 128.3 (all Ar-CH), 128.0, 127.7 (both CH), 71.1 (2-CH), 69.8 (5-CH), 30.8 (1′-CH_2), 21.9 (Ar-Me), and 10.6 (2′-Me); *m/z* (ES) 328 (M^+ + 1, 94%), 245 (5), 157 (7) and 102 (9) [Found: M^+ + 1, 328.1371].

(2*R*)-(*E*)-2-(*p*-Tolylsulfonylamino)non-4-ene 24e. (2*S*,3*R*,5*R*)-Iodopyrrolidine **37e** (25 mg, 0.07 mmol) in a mixture of ethanol (2.0 ml) and acetic acid (0.01 ml) was treated with zinc dust (0.325 mesh, 10 mg, 0.07 mmol). The resulting reaction mixture was stirred at ambient temperature for 6 h then filtered over Kieselguhr and the solid washed with dichloromethane (3 × 2 ml). The combined organic solutions were washed with 2 M aqueous sodium hydrogen carbonate (2 × 5 ml), then dried and the solvent evaporated to afford the *sulfonamide* **24e** (18.6 mg, 90%) as a viscous, yellow oil: $[\alpha]_D$ = +32.1 (*c* 0.008, $CHCl_3$); other spectral data were identical to those for the racemic sulfonamide **24d** (see above).

X-Ray crystallography for 37f, 36j and 37k †

Single crystals were obtained by vapour diffusion as described in the text; X-ray data were collected on a CAD4 diffractometer using monochromatized Mo-Kα radiation ($\lambda = 0.710\ 73$ Å).

(2*RS*,3*SR*,5*SR*)-2-Butyl-5-ethyl-3-iodo-1-*p*-tolylsulfonylpyrrolidine 37f. $C_{17}H_{26}INO_2S = 435.35$. Orthorhombic, $Pba2_1$ (No. 29), $a = 15.481(2)$, $b = 14.469(3)$, $c = 16.866(2)$ Å, $V = 3778(2)$ Å^3, $Z = 8.00$, $D_c = 1.531$ g cm^{-3}, $F(000) = 1760$. Crystal size $0.26 \times 0.18 \times 0.15$ mm. 15269 reflections were measured over the range $1.93 < \theta < 24.99°$ with $-1 \leqslant h \leqslant 18$, $-15 \leqslant k \leqslant 16$, $-18 \leqslant l \leqslant 15$ giving 5378 independent reflections [R(int) = 0.0761].

Full matrix least-squares refinement with all non-hydrogen atoms anisotropic and hydrogens in calculated positions. The maximum peak in the final ΔF map was 1.834 Å^{-3} and the minimum was −0.801 Å^{-3}. Final cycles of refinement gave $R = 0.0588$ and $R_w = 0.1252$.

(2*RS*,3*SR*,5*RS*)-5-Ethyl-3-iodo-2-phenyl-1-*p*-tolylsulfonylpyrrolidine 36j. $C_{19}H_{22}INO_2S = 455.34$. Monoclinic, $P2_1/n$, $a = 7.648$, $b = 13.629$, $c = 18.213$ Å, $\beta = 93.73(2)°$, $V = 1894.5$ Å^3, $Z = 4.00$, $D_c = 1.596$ g cm^{-3}, $F(000) = 912$. Crystal size $0.24 \times 0.22 \times 0.18$ mm. 7350 reflections were measured over the range $1.87 < \theta < 25.08°$ with $-8 \leqslant h \leqslant 8$, $-14 \leqslant k \leqslant 15$, $-21 \leqslant l \leqslant 21$ giving 2501 independent reflections [R(int) = 0.0507].

Full matrix least-squares refinement with all non-hydrogen atoms anisotropic and hydrogens in calculated positions. The maximum peak in the final ΔF map was 2.851 Å^{-3}. Final cycles of refinement gave $R = 0.0458$ and $R_w = 0.1082$.

(2*RS*,3*SR*,5*SR*)-5-Ethyl-3-iodo-2-phenyl-1-phenylsulfonylpyrrolidine 37k(i). $C_{18}H_{20}INO_2S = 441.31$. Monoclinic, $P2_1/c$, $a = 12.577(4)$, $b = 12.900(4)$, $c = 13.006(6)$ Å, $\beta = 119.06(2)°$, $V = 1844.5(12)$ Å^3, $Z = 4.00$, $D_c = 1.589$ g cm^{-3}, $F(000) = 880$. Crystal size $0.50 \times 0.50 \times 0.20$ mm. 3696 reflections were measured over the range $1.85 < \theta < 24.95$ with $0 \leqslant h \leqslant 14$, $0 \leqslant k \leqslant 15$, $-15 \leqslant l \leqslant 13$. A semi empirical absorption was applied (transmission factors 0.5123–0.7075) giving 3230 independent reflections [R(int) = 0.0643].

Full matrix least-squares refinement with all non-hydrogen atoms anisotropic and hydrogens in calculated positions. The maximum peak in the final ΔF map was 0.570 Å^{-3} and the minimum was −0.565 Å^{-3}. Final cycles of refinement gave $R = 0.0377$ and $R_w = 0.0992$.

(2*RS*,3*SR*,5*SR*)-5-Ethyl-3-iodo-2-phenyl-1-phenylsulfonylpyrrolidine 37k(ii). $C_{18}H_{20}INO_2S = 441.31$. Monoclinic, $P2_1/n$, $a = 14.617(3)$, $b = 14.417(3)$, $c = 8.616(2)$ Å, $\beta = 94.63(3)°$, $V = 1809.8(6)$ Å^3, $Z = 4.00$, $D_c = 1.620$ g cm^{-3}, $F(000) = 880$. Crystal size $0.60 \times 0.40 \times 0.20$ mm. 2851 reflections were measured over the range $1.99 < \theta < 22.95°$ with $0 \leqslant h \leqslant 16$, $0 \leqslant k \leqslant 15$, $-9 \leqslant l \leqslant 9$. A semi-empirical absorption was applied (transmission factors 0.6665–0.9724) giving 2501 independent reflections [R(int) = 0.0507].

Full matrix least-squares refinement with all non-hydrogen atoms anisotropic and hydrogens in calculated positions. The maximum peak in the final ΔF map was 0.767 Å^{-3} and the minimum was −0.722 Å^{-3}. Final cycles of refinement gave $R = 0.0410$ and $R_w = 0.1041$.

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References

1 J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 1976, 734; J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 1976, 738; for a discussion of why 5-*endo-trig* cyclisations are particularly unfavourable, see J. E. Baldwin, J. Cutting, W. Dupont, L. Kruse, L. Silberman and R. C. Thomas, *J. Chem. Soc., Chem. Commun.*, 1976, 736.
2 S. H. Kang and S. B. Lee, *Tetrahedron Lett.*, 1993, **34**, 1955; S. H. Kang and S. B. Lee, *Tetrahedron Lett.*, 1993, **34**, 7579; B. H. Lipshutz and J. C. Barton, *J. Am. Chem. Soc.*, 1992, **114**, 1084, but see ref. 7; E. D. Mihelich and G. A. Hite, *J. Am. Chem. Soc.*, 1992, **114**, 318; B. Lipshutz and T. Gross, *J. Org. Chem.*, 1995, **60**, 3572; M. E. Jung and C. J. Nichols, *Tetrahedron Lett.*, 1996, **37**, 7667; J. M. Barks, D. W. Knight and G. G. Weingarten, *J. Chem. Soc., Chem. Commun.*, 1994, 719; Y. Landais, D. Planchenault and V. Weber, *Tetrahedron Lett.*, 1995, **36**, 2987; O. Andrey, L. Ducry, Y. Landais, D. Planchenault and V. Weber, *Tetrahedron*, 1997, **53**, 4338.
3 S. B. Bedford, K. E. Bell, F. Bennett, C. J. Hayes, D. W. Knight and D. E. Shaw, *J. Chem. Soc., Perkin Trans. 1*, 1999, 2143.
4 K. E. Harding and T. H. Tiner, *Comprehensive Organic Synthesis*, Eds. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, vol. 4, 363; P. A. Bartlett, *Asymmetric Synthesis*, Ed. J. D. Morrison, Academic Press, Orlando, 1984, **3**, 144; G. Cardillo and M. Orena, *Tetrahedron*, 1990, **46**, 3321.
5 S. P. Bew, J. M. Barks, D. W. Knight and R. J. Middleton, *Tetrahedron Lett.*, 2000, **41**, 4447; S. P. Bew, D. W. Knight and R. J. Middleton, *Tetrahedron Lett.*, 2000, **41**, 4453.
6 D. W. Knight, A. L. Redfern and J. Gilmore, *Tetrahedron Lett.*, 1998, **39**, 8909.
7 J. M. Barks, D. W. Knight, C. J. Seaman and G. G. Weingarten, *Tetrahedron Lett.*, 1994, **35**, 7259; J. M. Barks, D. W. Knight and G. G. Weingarten, *J. Chem. Soc., Perkin Trans. 1*, 2000, 3469.
8 For a preliminary report, see A. D. Jones and D. W. Knight, *Chem. Commun.*, 1996, 915.
9 H. Tsubomura and S. Nagakura, *J. Chem. Phys.*, 1957, **27**, 819; S. Nagakura, *J. Am. Chem. Soc.*, 1958, **80**, 520; O. Hassel and C. Rømming, *Quart. Rev.*, 1962, **16**, 1; C. D. Schmulbach and D. M. Hart, *J. Am. Chem. Soc.*, 1964, **86**, 2347; C. Biselx, J.-J. Schaer and D. Janjic, *Helv. Chim. Acta*, 1978, **61**, 832; A. Goosen, C. W. McCleland and A. W. Sipamla, *J. Chem. Res. (M)*, 1995, **18**, 0311.
10 S. Knapp and A. T. Levorse, *J. Org. Chem.*, 1988, **53**, 4006; S. Knapp and F. S. Gibson, *Org. Synth.*, 1992, **70**, 101; see also A. Bongini, G. Cardillo, M. Orena, S. Sandri and C. Tomasini, *J. Org. Chem.*, 1986, **51**, 4905; A. Bongini, G. Cardillo, M. Orena, S. Sandri and C. Tomasini, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1339; M. J. Kurth and S. H. Bloom, *J. Org. Chem.*, 1989, **54**, 411.
11 H. Takahata, T. Takamatsu and T. Yamazaki, *J. Org. Chem.*, 1989, **54**, 4812; H. Takahata, T. Takamatsu, M. Mozumi, Y.-S. Chen, T. Yamazaki and K. Aoe, *J. Chem. Soc., Chem. Commun.*, 1987, 1627; H. Takahata, T. Suzuki, M. Maruyama, K. Moriyama, M. Mozumi, T. Takamatsu and T. Yamazaki, *Tetrahedron*, 1988, **44**, 4777; S. Kano, T. Yokomatsu, H. Iwasawa and S. Shibuya, *Heterocycles*, 1987, **26**, 359.
12 H. Takahata and T. Yamazaki, *Heterocycles*, 1988, **27**, 1953.
13 Y. Tamura, S.-i. Kawamura, T. Bando, K. Tanaka, M. Hojo and Z.-i. Yoshida, *J. Org. Chem.*, 1988, **53**, 5491. For a related Pd-catalysed process with the same substrates, see Y. Tamaru, M. Hojo and Z.-i. Yoshida, *J. Org. Chem.*, 1988, **53**, 5731; see also A. Hirama, M. Iwashita, Y. Yamazaki and S. Ito, *Tetrahedron Lett.*, 1984, **25**, 4963; S. Kobayashi, T. Isobe and M. Ohno, *Tetrahedron Lett.*, 1984, **25**, 5079; A. Bongini, G. Cardillo, M. Orena, G. Porzi and S. Sandri, *Chem. Lett.*, 1988, 87.
14 D. R. Williams, M. H. Osterhout and J. M. McGill, *Tetrahedron Lett.*, 1989, **30**, 1327; D. R. Williams, M. H. Osterhout and J. M. McGill, *Tetrahedron Lett.*, 1989, **30**, 1331.
15 A. J. Biloski, R. D. Wood and B. Ganem, *J. Am. Chem. Soc.*, 1982, **104**, 3233.
16 T. Aida, R. Legault, D. Dugat and T. Durst, *Tetrahedron Lett.*, 1979, 4993.
17 O. Sakurai, M. Takashi, T. Ogiku, M. Hayashi, H. Horikawa and T. Iwakaki, *Tetrahedron Lett.*, 1994, **35**, 6317.
18 S. Takano, Y. Iwabuchi and K. Ogasawara, *J. Chem. Soc., Chem. Commun.*, 1988, 1527; S. Takano, Y. Iwabuchi and K. Ogasawara,

Heterocycles, 1989, **29**, 1861; S. Takano, M. Moriya, Y. Iwabuchi and K. Ogasawara, *Tetrahedron Lett.*, 1989, **30**, 3805.
19 M. Tiecco, L. Testaferri, M. Tingoli, D. Bartoli and R. Balducci, *J. Org. Chem.*, 1990, **55**, 429.
20 K. C. Nicolaou, D. A. Claremon, W. E. Barnette and S. P. Seitz, *J. Am. Chem. Soc.*, 1979, **101**, 3704; K. C. Nicolaou, *Tetrahedron*, 1981, **37**, 4097; D. L. J. Clive, V. Farina, A. Singh, C. K. Wong, W. A. Kiel and S. M. Menchen, *J. Org. Chem.*, 1980, **45**, 2120; R. R. Webb II and S. Danishefsky, *Tetrahedron Lett.*, 1983, **24**, 1357.
21 S. Danishefsky, E. M. Berman, M. Ciufolini, S. J. Etheridge and B. E. Segmuller, *J. Am. Chem. Soc.*, 1985, **107**, 3891.
22 A. Toshimitsu, K. Terao and S. Vemura, *J. Org. Chem.*, 1986, **51**, 1724.
23 K. Terao, A. Toshimitsu and S. Vemura, *J. Chem. Soc.*, *Perkin Trans. 1*, 1986, 1837; see also A. Toshimitsu, K. Terao and S. Vemura, *J. Chem. Soc.*, *Chem. Commun.*, 1986, 530; A. Toshimitsu, K. Terao and S. Vemura, *Tetrahedron Lett.*, 1984, **25**, 5917; S. Saito, H. Tamai, Y. Usui, M. Inaba and T. Moriwake, *Chem. Lett.*, 1984, 1243.
24 J. J. Perie, J. P. Laval, J. Roussel and A. Lattes, *Tetrahedron*, 1972, **28**, 675.
25 M. Tokuda, Y. Yamada and H. Suginome, *Chem. Lett.*, 1988, 1289.
26 K. E. Harding and S. R. Burks, *J. Org. Chem.*, 1981, **46**, 3920; K. E. Harding and T. H. Marman, *J. Org. Chem.*, 1984, **49**, 2838; R. H. Schlessinger and E. J. Iwanowicz, *Tetrahedron Lett.*, 1987, **28**, 2083; H. Takahta, H. Takehara, N. Ohkubo and T. Momose, *Tetrahedron: Asymmetry*, 1990, **1**, 561; see also K. E. Harding, T. H. Marman and D. Nam, *Tetrahedron*, 1988, **44**, 5605; P. S. Liu, *J. Org. Chem.*, 1987, **52**, 4717.
27 J. Barluenga, C. Jiminez, C. Najera and M. Yus, *J. Chem. Soc.*, *Perkin Trans. 1*, 1984, 721.
28 Z. K. M. Abd El Samii, M. I. Al Ashmawy and J. M. Mellor, *J. Chem. Soc.*, *Perkin Trans. 1*, 1988, 2517.
29 G. Cappozi, R. Ottana and G. Romeo, *Heterocycles*, 1986, **24**, 583.
30 I. Coldham and S. Warren, *J. Chem. Soc.*, *Perkin Trans. 1*, 1993, 1637; K. Chibale and S. Warren, *J. Chem. Soc.*, *Perkin Trans. 1*, 1995, 2411.
31 T. Ohsawa, M. Ihara, K. Fukumoto and T. Kametani, *J. Org. Chem.*, 1983, **48**, 3644.
32 Y. Tamaru, T. Kobayashi, S. Kawamura, H. Ochiai and Z. Yoshida, *Tetrahedron Lett.*, 1985, **26**, 4479; Y. Tamaru, M. Hojo, S. Kawamura and Z. Yoshida, *J. Org. Chem.*, 1986, **51**, 4089; R. C. Larock, T. R. Hightower, L. A. Hasvold and K. P. Peterson, *J. Org. Chem.*, 1996, **61**, 3584; L. S. Hegedus and J. M. McKearnin, *J. Am. Chem. Soc.*, 1992, **104**, 2444; I. W. Davies, D. I. Scopes and T. Gallagher, *Synlett*, 1993, 85; T. Gallagher, I. W. Davies, S. W. Jones, D. Lathbury, M. F. Mahon, K. C. Molloy, R. W. Shaw and P. Vernon, *J. Chem. Soc.*, *Perkin Trans. 1*, 1992, 433; P. Vernon and T. Gallagher, *J. Chem. Soc.*, *Chem. Commun.*, 1987, 245; N. Kurokawa and Y. Ohfune, *J. Am. Chem. Soc.*, 1986, **108**, 6041; Y. Ohfune, K. Hori and M. Sakaintani, *Tetrahedron Lett.*, 1986, **27**, 6079; M. R. Gagne and T. J. Marks, *J. Am. Chem. Soc.*, 1989, **111**, 4108.
33 See, for example, S. Knapp and D. V. Patel, *J. Am. Chem. Soc.*, 1983, **105**, 6985; S. Knapp and D. V. Patel, *J. Org. Chem.*, 1984, **49**, 5072; G. Rajendra and M. J. Miller, *J. Org. Chem.*, 1987, **52**, 4471; M. Ihara, Y. Haga, M. Yonekura, T. Ohsawa, K. Fukumoto and T. Kametani, *J. Am. Chem. Soc.*, 1983, **105**, 7345.
34 O. Mitsunobu, *Synthesis*, 1981, 1; O. Mitsunobu, *Comprehensive Organic Synthesis*, Eds. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, vol. 6, 1; O. Mitsunobu, *Comprehensive Organic Synthesis*, Eds. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, vol. 6, 65; D. L. Hughes, *Org. React.*, 1992, **42**, 335. For the use of phthalimide, see O. Mitsunobu, M. Wada and T. Sano, *J. Am. Chem. Soc.*, 1972, **94**, 679.
35 J. R. Henry, L. R. Marcin, M. C. McIntosh, P. M. Scola, G. D. Harris, Jun. and S. M. Weinreb, *Tetrahedron Lett.*, 1989, **30**, 5709.
36 M. Yamaguchi and I. Hirao, *Tetrahedron Lett.*, 1982, **33**, 391.
37 H. Leidner and E. Zbiral, *Helv. Chim. Acta*, 1977, **60**, 417; E. Fabiano, B. T. Golding and M. M. Sadeghi, *Synthesis*, 1987, 190; B. Lal, B. N. Pramanik, M. S. Manhas and A. K. Bose, *Tetrahedron Lett.*, 1977, 1977; M. C. Viaud and P. Rollin, *Synthesis*, 1990, 130.
38 R. E. Ireland, R. H. Mueller and A. K. Willard, *J. Am. Chem. Soc.*, 1976, **98**, 2868.
39 K. Ninomiya, T. Shioiri and S. Yamada, *Tetrahedron*, 1974, **30**, 2151; K. Ninomiya, T. Shioiri and S. Yamada, *Chem. Pharm. Bull.*, 1974, **22**, 1398.
40 M. S. Blum, *Chemical Defenses of Arthropods*, Academic Press, New York, 1981.
41 D. J. Pedder, H. M. Fales, T. Jaouni, M. S. Blum, J. MacConnell and R. M. Crewe, *Tetrahedron*, 1976, **32**, 2275; T. H. Jones, M. S. Blum and H. M. Fales, *Tetrahedron Lett.*, 1979, 1031; M. S. Blum, T. H. Jones, B. Hölldobler, H. M. Fales and T. Jaouni, *Naturwissenschaften*, 1980, **67**, 144.
42 H. Günther, *NMR Spectroscopy*, 2nd edn., Georg Thieme Verlag, Stuttgart, 1992; H. Günther, *NMR Spectroscopy*, 2nd edn., English translation, John Wiley and Sons Ltd., Chichester, 1995.
43 H. Takahata, H. Takehara, N. Ohkubo and T. Momose, *Tetrahedron: Asymmetry*, 1990, **1**, 561; J.-E. Backvall, H. E. Schink and Z. D. Renko, *J. Org. Chem.*, 1990, **55**, 826; N. Machinaga and C. Kibayashi, *J. Org. Chem.*, 1991, **56**, 1386.
44 We are very grateful to Professor M. B. Hursthouse for the provision of facilities for obtaining these data.
45 P. A. Bartlett and J. Myerson, *J. Am. Chem. Soc.*, 1978, **100**, 3950.
46 W. S. Lee, K. C. Jang, J. H. Kim and K. H. Park, *Chem. Commun.*, 1999, 251.
47 D. W. Knight, A. L. Redfern and J. Gilmore, *Synlett*, 1998, 731.
48 A. D. Jones, D. W. Knight, A. L. Redfern and J. Gilmore, *Tetrahedron Lett.*, 1999, **40**, 3267.
49 W. L. F. Armarego and D. D. Perrin, *Purification of Laboratory Chemicals*, Butterworth Heinemann, Oxford, 1996.
50 R. E. Doolittle and R. R. Heath, *J. Org. Chem.*, 1984, **49**, 5041; T. Mukhopadhyay and D. Seebach, *Helv. Chim. Acta*, 1982, **65**, 385.
51 E.-i. Negishi, *J. Chem. Soc.*, *Chem. Commun.*, 1976, 17; B. R. Neustadt, *Tetrahedron Lett.*, 1994, **35**, 379; J. A. Campbell and D. J. Hart, *J. Org. Chem.*, 1993, **58**, 2900.
52 G. Kresze and U. Wagner, *Liebigs Ann. Chem.*, 1972, 93.
53 A. Mosandl and V. Schubert, *J. Essent. Oil Res.*, 1990, **3**, 121.