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On the α-lithiation-rearrangement of *N*-toluensulfonyl aziridines: mechanistic and synthetic aspects

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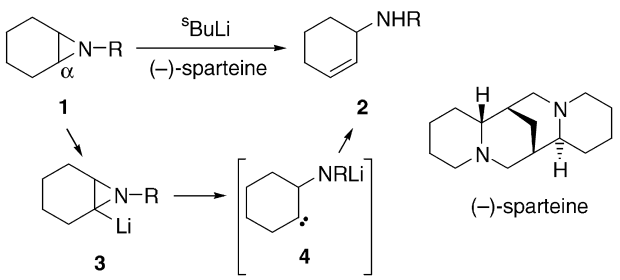
Abstract—A detailed study of the rearrangement of five cycloalkene *N*-toluenesulfonyl (tosyl) aziridines using *sec*-butyllithium (with and without added ligands such as (−)-sparteine and TMEDA) has been carried out. Allylic sulfonamides were the main products from the cyclopentene and cyclohexene aziridines whereas bicyclic sulfonamides were obtained from the cycloheptene and cyclooctene aziridines. In most cases, *p*-toluenesulfonamide ($TsNH_2$) was produced as a by-product and a mechanistic explanation for its formation is forwarded. These reactions are believed to involve α-lithiation to a lithiated aziridine which can then partition through two pathways: (i) rearrangement to allylic or bicyclic sulfonamides via C–H insertion reactions or (ii) reductive alkylation to alkenes via attack by *sec*-butyllithium and subsequent elimination of $TsNH_2$. In the (−)-sparteine reactions, the products were generated with 38–66% ee and the sense of asymmetric induction involved lithiation of the *S*-aziridine stereocentre. This is opposite to that observed with epoxides.

1. Introduction

Lithiated epoxides (oxiranyl anions) were first identified as reaction intermediates by Cope in 1951 to explain the conversion of cyclooctatetraene into 2,4,6-cyclooctatrien-1-one.[1] Since then, the chemistry of lithiated epoxides has blossomed into a significant research area with major worldwide interest.[2,3] Of recent interest, Hodgson and co-workers have developed elegant and useful asymmetric methodology based on enantioenriched lithiated epoxides, generated by direct α-lithiation of epoxides using alkyllithiums in the presence of chiral ligands such as (−)-sparteine and bisoxazolines.[3–5] In contrast, the chemistry of lithiated aziridines (aziridinyl anions) produced by direct α-lithiation/deprotonation has received much less attention.[2] Of the known examples, most lithiated aziridines are generated from aziridines equipped with an anion stabilising group (e.g. acyl,[6] alkenyl,[7] oxazolinyl,[8] benzotriazoyl[9] or sulfonyl[10] groups) attached directly. However, there are three reported instances of lithiated aziridines generated from aziridines lacking an anion stabilising group: Müller's α-lithiation-rearrangement of *N*-toluenesulfonyl (tosyl) aziridines,[11] Vedejs' α-lithiation of borane complexes of *N*-alkyl aziridines[12] and Beak's α-lithiation-in situ trapping of *N*-Boc aziridines.[13] It is these reports that attracted our attention for the present study.

For some time, we have been intrigued by the prospect of developing suitable reagents/conditions for the direct conversion of aziridines into allylic amines, exemplified by the rearrangement of **1** into **2** (Scheme 1). The analogous rearrangement of epoxides to allylic alcohols is well known and has been widely studied using chiral lithium amide bases,[14,15] including contributions from our group.[16] However, there are only three reports[11,17,18] of the direct, one-step transformation of aziridines into protected allylic amines and lithium amides alone have not been reported to carry out this interconversion.[16a] Of these, Scheffold[17] used a Vitamin B_{12}-catalysed process whilst the two most recent reports (Müller[11] and Mordini[18a]) utilised strong bases (e.g. *sec*-butyllithium/(−)-sparteine, LDA/potassium *tert*-butoxide or *n*-butyllithium/potassium *tert*-butoxide) to convert *N*-tosyl aziridine **1** (R=Ts) into allylic sulfonamide **2** (R=Ts).

In his original report, Müller reported three examples of the rearrangement of *N*-tosyl aziridines (e.g. **1**, R=Ts) using



Scheme 1.

Keywords: aziridines; sulfonamides; rearrangement; lithiation; carbenes and carbenoids.
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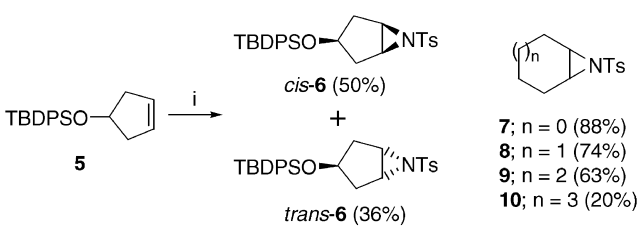
sec-butyllithium/(−)-sparteine.[11] By analogy with the extensive literature on epoxides,[2,3] it is likely that *sec*-butyllithium/(−)-sparteine would cause aziridines **1** to undergo irreversible α-lithiation to give lithiated aziridines **3** (aziridinyl anions) which will presumably possess carbenoid character (Scheme 1). Subsequent insertion into an adjacent C–H bond either directly or via the carbene **4** (generated by α-elimination of lithiated aziridine **3**) would then produce allylic amines **2**. It may well be that Mordini's reactions[18a] of *N*-tosyl aziridines with LDA/postassium *tert*-butoxide or *n*-butyllithium/potassium *tert*-butoxide also proceed via a similar α-lithiation mechanism, although Mordini suggests a β-elimination process (reactions of lithium amides with epoxides can proceed via α- or β-lithiation mechanisms, depending strongly on the epoxide structure and reaction conditions[19]). Due to our ongoing interest in sparteine-like diamines[20] and aziridines,[16a,21] coupled with our desire to develop the aziridine to allylic amine reaction, we became interested in further exploiting Müller's seminal contribution. Thus, we have carried out a study on the reaction of alkyllithiums with five cycloalkene *N*-tosyl aziridines and full results are presented in this paper.[22] Of particular significance, we have established the sense of asymmetric induction in the lithiation of *N*-tosyl aziridines with (−)-sparteine and we have rationalised the formation of *p*-toluenesulfonamide ($TsNH_2$) as a by-product in these reactions. The formation of $TsNH_2$ has allowed us to provide evidence in support of the intermediacy of lithiated aziridines **3** in the rearrangement reactions discussed. Additionally, our results indicate a significant ligand effect and this has allowed us to draw some important synthetic conclusions.

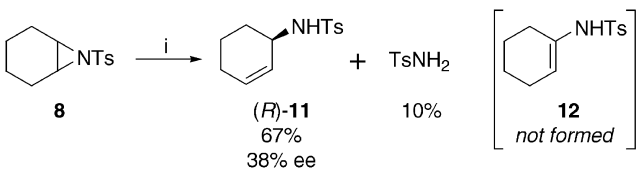
2. Results and discussion

As substrates for the detailed α-lithiation rearrangement study, we have utilised *N*-tosyl aziridines *cis*-**6** and **7**–**10** and the aziridines were prepared in one step from the corresponding cycloalkenes. Of the methods available (e.g. iodinane-based procedures[23] and Chloramine-T-based conditions[24,25]), we prefer the Sharpless protocol[25] (Chloramine-T, phenyltrimethylammonium tribromide, acetonitrile, room temperature) as it is a generally high yielding and simple method. For example, alkene **5** was converted into a separable mixture of aziridines *cis* and *trans*-**6** (relative stereochemistry established by independent synthesis from a known epoxide[21]) in a high 86% combined yield using the Sharpless conditions (Scheme 2). In a similar way, simpler *N*-tosyl aziridines **7**–**9** were prepared in high yields (63–88%, Scheme 2) but, unfortunately, this procedure was less successful with cyclooctene, resulting in a lower yield (20%) of aziridine **10** (Scheme 2).



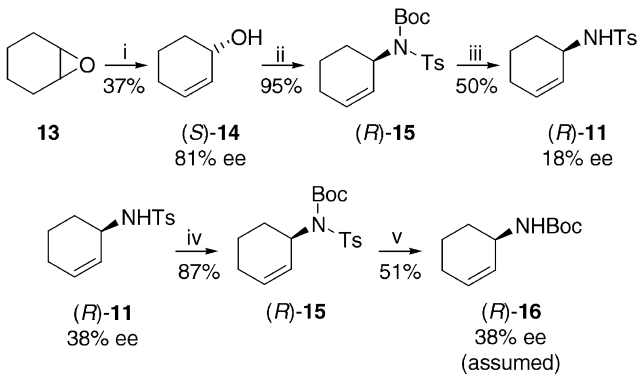
Scheme 2. *Reagents and conditions*: (i) 1.1 equiv. $TsNCl^-Na^+\cdot 3H_2O$, 0.1 equiv. $PhMe_3N^+Br_3^-$, MeCN, rt, 16 h.

As a starting point in our study, we selected cyclohexene *N*-tosyl aziridine **8** and conditions that were essentially the same as those reported by Müller and Nury for their aziridine rearrangements.[11] Thus, a diethyl ether solution of *N*-tosyl aziridine **8** was added to 2.9 equiv. of *sec*-butyllithium/(−)-sparteine in diethyl ether at −78°C. After 4 h at −78°C, the solution was allowed to warm to room temperature (over approximately 1 h) and worked up. Purification by flash chromatography furnished allylic sulfonamide (*R*)-**11** in 67% yield (38% ee by chiral HPLC) and *p*-toluenesulfonamide ($TsNH_2$) in 10% yield (Scheme 3). The enantioselectivity was virtually identical to that reported by Müller but there were some differences: (i) our isolated yield (typically 60–70%) was approximately 30% higher than that reported by Müller; (ii) we have no evidence for the generation of the isomeric enamide **12** (despite having run the reaction many times and carefully analysing the crude product mixtures by ^1H NMR spectroscopy) and (iii) our reaction was always accompanied by the formation of some $TsNH_2$. Upon subsequent re-examination by Müller and co-workers, all of our observations (i)–(iii) listed above have now been verified.[26]



Scheme 3. *Reagents and conditions*: (i) 2.9 equiv. ^{s}BuLi, 2.9 equiv. (−)-sparteine, Et_2O, −78°C, 4 h then to rt over 1 h.

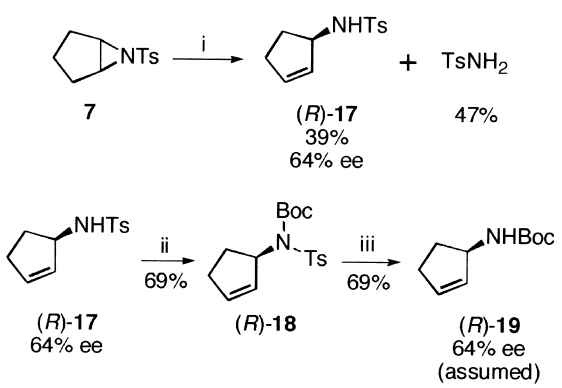
The major enantiomer of allylic sulfonamide **11** generated from the *sec*-butyllithum/(−)-sparteine reaction was established as (*R*) using two different reaction sequences (Scheme 4). In a first sequence, we attempted to prepare allylic sulfonamide (*R*)-**11** via a Mitsunobu route using Weinreb's TsNHBoc reagent[27] and allylic alcohol (*S*)-**14**. Thus, cyclohexene oxide **11** was rearranged using the chiral



Scheme 4. *Reagents and conditions*: (i) 2 equiv. (1*R*,2*S*)-*N*-methyl-1-phenyl-2-(1-pyrrolidinyl)-1-propanamine, 2 equiv. ^{n}BuLi, THF, 0°C to rt over 1 h then 16 h at rt; (ii) 1.5 equiv. TsNHBoc, 2.5 equiv. DEAD, 3.0 equiv. PPh_3, THF, rt, 10 h; (iii) TFA, CH_2Cl_2, 0°C to rt over 1 h; (iv) 1.1 equiv. Boc_2O, 1.1 equiv. Et_3N, 0.1 equiv. DMAP, CH_2Cl_2, rt, 16 h; (v) 10 equiv. Na, NH_3, THF, −78°C for 1 h then rt for 1 h.

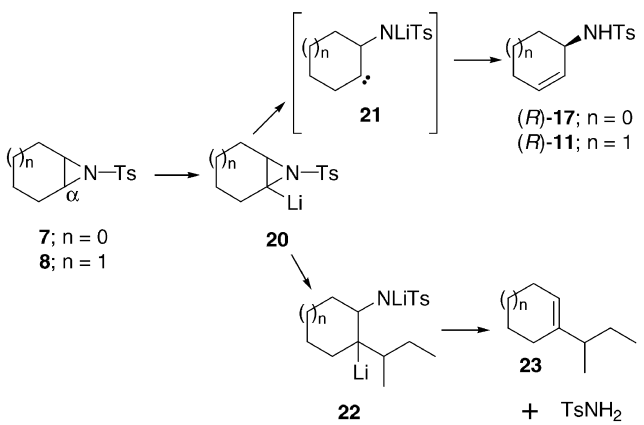
lithium amide derived from (1*R*,2*S*)-*N*-methyl-1-phenyl-2-(1-pyrrolidinyl)-1-propanamine (independently developed by ourselves[28] and Ahlberg[29]) to give allylic alcohol (*S*)-**14** of 81% ee (determined by Mosher's ester formation). The moderate isolated yield (37%) of allylic alcohol (*S*)-**14** presumably reflects its volatility. Then, (*S*)-**14** was subjected to a standard Mitsunobu reaction with TsNHBoc to generate a high yield (95%) of protected allylic sulfonamide (*R*)-**15**. Subsequent Boc deprotection gave allylic sulfonamide (*R*)-**11** in 50% yield but of only 18% ee (by chiral HPLC). We suggest that the enantiomeric excess of (*S*)-**14** is compromised significantly during the Mitsunobu reaction by a competing S_N2' reaction in this sterically unbiased system. This has precedent in related Mitsunobu reactions with carboxylic acids.[30] In contrast, in sterically biased systems, Mitsunobu reactions of cyclic allylic alcohols proceed with essentially complete stereochemical integrity, as we have observed for other nitrogen-based Mitsunobu reactions.[16a] Due to this non-stereospecific Mitsunobu reaction, we sought unequivocal assignment of absolute stereochemistry in allylic sulfonamide **11** and a straightforward second route was investigated. Allylic sulfonamide **11** of 38% ee was Boc protected to give (*R*)-**15** from which (*R*)-**16** was formed by tosyl deprotection using sodium in liquid ammonia. The absolute stereochemistry of Boc protected allylic amine (*R*)-**16** was assigned by comparison of its optical rotation {$[\alpha]_D$=+30.0 (*c* 1.1 in $CHCl_3$), 38% ee assumed} with the literature value[17] {$[\alpha]_D$=+101 (*c* 2.8 in $CHCl_3$) for (*R*)-**16**, 95% ee}. Hence, the major enantiomer generated from the rearrangement of *N*-tosyl aziridine **8** was unequivocally assigned as allylic sulfonamide (*R*)-**11**.

Next, the previously unstudied cyclopentene *N*-tosyl aziridine **7** was rearranged using 2.9 equiv. of *sec*-butyllithium/(−)-sparteine (same conditions as in Scheme 3). In this case, a 39% yield of allylic sulfonamide (*R*)-**17** (64% ee by chiral HPLC) was obtained (Scheme 5). Compared to the cyclohexene aziridine **8**, the yield of allylic sulfonamide (*R*)-**17** was lower (39%) and was accompanied by an increase in the yield of the $TsNH_2$ by-product (47%); the enantioselectivity was higher (64% ee) and the same sense of asymmetric induction was observed. The major enantiomer of allylic sulfonamide **17** was assigned as (*R*) using the sequence outlined in Scheme 5. Thus, Boc protection gave (*R*)-**18** and subsequent tosyl deprotection generated Boc protected allylic amine (*R*)-**19**. Comparison of its optical rotation {$[\alpha]_D$=+38.8 (*c* 1.0 in CH_2Cl_2), 64% ee assumed} with that reported in the literature[17] {$[\alpha]_D$=+77.0 (*c* 5.1 in CH_2Cl_2) for (*R*)-**19**, 87% ee} enabled the stereochemistry to be assigned.



Scheme 5. *Reagents and conditions*: (i) 2.9 equiv. ^{s}BuLi, 2.9 equiv. (−)-sparteine, Et_2O, −78°C, 4 h then to rt over 1 h; (ii) 1.1 equiv. Boc_2O, 1.1 equiv. Et_3N, 0.1 equiv. DMAP, CH_2Cl_2, rt, 16 h; (iii) 10 equiv. Na, NH_3, THF, −78°C for 1 h then rt for 1 h.

At this stage, it is appropriate to consider the likely mechanisms that could account for the formation of the allylic sulfonamides (*R*)-**11** and (*R*)-**17** as well as the $TsNH_2$ by-product. The formation of $TsNH_2$ had not been noted in Müller's original report[11] and we were especially keen to rationalise the generation of $TsNH_2$ as both of the C–N bonds of the aziridines must have been cleaved. A proposed mechanistic outline is delineated in Scheme 6. Irreversible α-lithiation of the *N*-tosyl aziridines **7** and **8** by *sec*-butyllithium/(−)-sparteine would produce lithiated aziridines **20**. Subsequent insertion into the adjacent C–H bond either directly or via the carbenes **21** (generated by α-elimination of lithiated aziridines **20**) would produce the allylic sulfonamides (*R*)-**17** and (*R*)-**11** after aqueous work-up. However, by analogy with their epoxide cousins, lithiated aziridines **20** are also likely to possess significant electrophilic character and this opens up another possible reaction pathway. Attack of lithiated aziridines **20** by a second equivalent of *sec*-butyllithium would lead to dilithiated adducts **22** from which elimination of $TsNLi_2$ would generate alkenes **23** and $TsNH_2$ after aqueous work-up (Scheme 6). We believe that this is the mechanistic process that accounts for the generation of $TsNH_2$ in our reactions. Such a reductive alkylation process is well documented for lithiated epoxides and was first proposed by Crandall and Lin in 1967.[31] Since then, Mioskowski[32,33] and, more recently, Hodgson[3,5a,b,34] have widely utilised this type of reductive alkylation process with lithiated epoxides in synthetic applications. Of particular relevance to our mechanistic conjecture, Mioskowski et al. reported the conversion of epoxides into substituted alkenes via reductive alkylation of lithiated epoxides with concomitant elimination of Li_2O.[32]



Scheme 6.

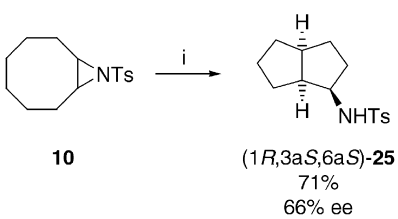
The reductive alkylation of lithiated aziridines (and hence the formation of $TsNH_2$) has not been described previously. Unfortunately, we have been unable to isolate alkenes **23** (*n*=0 and 1) from the *sec*-butyllithium/(−)-sparteine reactions of aziridines **7** and **8**. Thus, in order to provide

Scheme 7. *Reagents and conditions*: (i) 2.9 equiv. ^{s}BuLi, Et_2O or THF, −78°C, 4 h then to rt over 1 h.

further evidence in support of our mechanistic rationale, we decided to study the reaction of *N*-tosyl aziridine *cis*-**6** as this should generate a non-volatile alkene **24**. Based on Mioskowski's precedent with epoxides,[32] it appeared likely that the reductive alkylation pathway would be dominant if the reaction was carried out in the absence of ligand. Therefore, aziridine *cis*-**6** was treated with 2.9 equiv. of *sec*-butyllithium alone in Et_2O under the usual reactions conditions and, after work-up and chromatography, a 76% yield of substituted alkene **24** (50:50 mixture of diastereomers) was isolated. The same reaction proceeded with 70% yield in THF. From both of these reactions, $TsNH_2$ was also produced and there was no evidence for the formation of any allylic sulfonamide. These are the first examples of the preparation of substituted alkenes by the reductive alkylation of lithiated aziridines and this type of process could have useful synthetic applications. Of greater significance to the present work, the reactions with aziridine *cis*-**6** strongly support our mechanistic speculation regarding the generation of $TsNH_2$.

The *sec*-butyllithium/(−)-sparteine reactions of the cycloheptene and cyclooctene *N*-tosyl aziridines (**9** and **10**) have also been studied. Surprisingly, under the usual conditions with *sec*-butyllithium/(−)-sparteine, the cycloheptene aziridine **9** did not produce any allylic sulfonamide and we were unable to isolate any meaningful products from this reaction. In contrast, the cyclooctene aziridine **10** was well-behaved and underwent rearrangement to the bicyclic sulfonamide **25**, as expected based on previous epoxide[4] and aziridine[11] results. From the reaction of aziridine **10**, a 71% yield of bicyclic sulfonamide (1*R*,3a*S*,6a*S*)-**25** (66% ee by chiral HPLC) was isolated after chromatography. There was no evidence of $TsNH_2$ being generated from this reaction and our reaction exhibits comparable yield and enantioselectivity to those reported by Müller.[11]

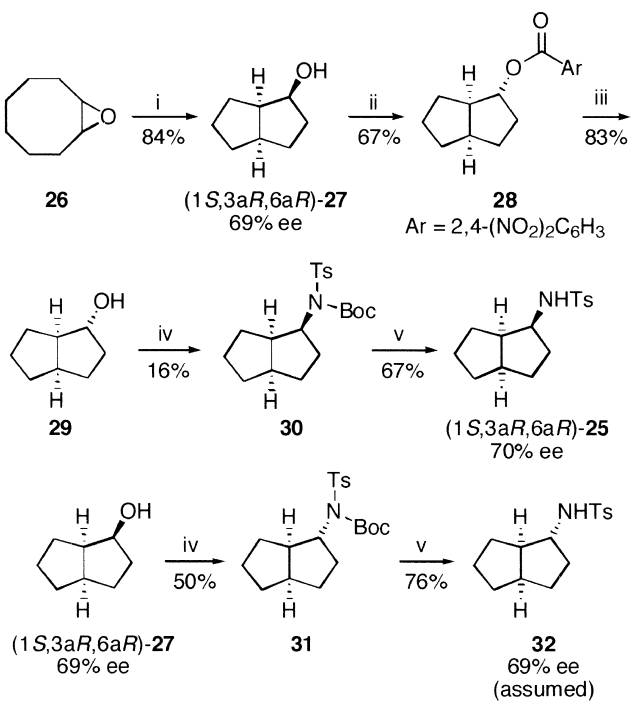
The relative and absolute stereochemistry of the bicyclic sulfonamide **25** generated from the (−)-sparteine reaction was established via a series of Mitsunobu reactions starting from alcohol (1*S*,3a*R*,6a*R*)-**27**, as outlined in Scheme 9. It is worth emphasising that in all of these Mitsunobu reactions, there was no evidence for the formation of other



Scheme 8. *Reagents and conditions*: (i) 2.9 equiv. ^{s}BuLi, 2.9 equiv. (−)-sparteine, Et_2O, −78°C, 4 h then to rt over 1 h.

diastereomeric products. Using Hodgson's conditions,[4] cyclooctene oxide **26** was rearranged with *sec*-butyllithium/(−)-sparteine to give bicyclic alcohol (1*S*,3a*R*,6a*R*)-**27** (69% ee by chiral HPLC of a derivative) in 84% yield. In order to generate the same relative stereochemistry in bicyclic sulfonamide **25**, initial inversion of the hydroxyl configuration in **27** followed by substitution with an amino group (i.e. a second inversion) would be required.

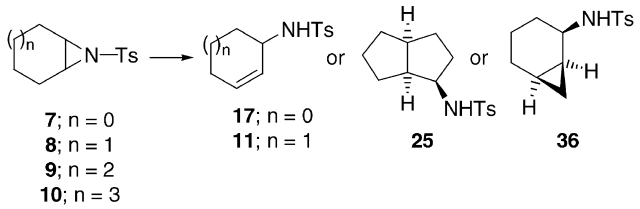
Thus, alcohol (1*S*,3a*R*,6a*R*)-**27** was converted into the 2,4-dinitrobenzoate **28** using a Mitsunobu reaction and thence into alcohol **29** upon treatment with potassium hydroxide. Introduction of the amino group was achieved using a Mitsunobu reaction with TsNHBoc to give sulfonamide **30** in 16% yield. The low yield of this reaction (despite an extended reaction time of 64 h) reflects the difficulty in carrying out S_N2 substitution on the sterically hindered *endo* face of the bicyclic system. An interesting reactivity comparison was obtained when the same Mitsunobu reaction was carried out with the diastereomeric alcohol **27**—in this case, we isolated a satisfactory 50% yield of the Mitsunobu adduct **31** (clearly distinguishable from **30** by ^{1}H and ^{13}C NMR spectroscopic data—see Section 4) via S_N2 attack on the more accessible *exo* face. Deprotection of the Boc group in sulfonamide **30** gave (1*S*,3a*R*,6a*R*)-**25** (70% ee by chiral HPLC) of known absolute and relative stereochemistry. As expected, its ^{1}H and ^{13}C NMR spectra were identical to the bicyclic sulfonamide generated from the *sec*-butyllithium/(−)-sparteine rearrangement of aziridine **10**. However, its sign of optical rotation was opposite to that obtained from the aziridine rearrangement reaction. For final confirmation of the relative stereochemistry, **31** was Boc deprotected to give



Scheme 9. (i) 2.4 equiv. ^{s}BuLi, 2.4 equiv. (−)-sparteine, Et_2O, −78°C, 5 h then to rt over 16 h; (ii) 1.5 equiv. 2,4-dinitrobenzoic acid, 2.5 equiv. DEAD, 3.0 equiv. PPh_3, THF, rt, 64 h; (iii) KOH, water–MeOH–THF, 0°C, 30 min; (iv) 1.5 equiv. TsNHBoc, 2.5 equiv. DEAD, 3.0 equiv. PPh_3, THF, rt, 64 h; (v) TFA, CH_2Cl_2, 0°C to rt then rt for 2.5 h.

bicyclic sulfonamide **32**, whose ^{1}H and ^{13}C NMR spectra were different to those of **25** recorded by us and reported by Müller[11] (for **25**, CHN signal is at δ_H 3.62–3.51 (m) and δ_C 57.0;[11] for **32**, CHN signal is at δ_H 3.13 (br quin., J=7.0 Hz) and δ_C 61.4).

The sense of asymmetric induction in the rearrangement of aziridines **7**, **8** and **10** using *sec*-butyllithium/(−)-sparteine has been unequivocally established in the work presented so far. In each case, the sense of induction is the same: preferential lithiation of the *S*-aziridine stereocentre occurs to give lithiated aziridines **20** (Fig. 1) In the one example where the stereoselectivity was established, Müller[11] found that a norbornene-derived *N*-tosyl aziridine rearranged via lithiated aziridine **35** (Fig. 1), also generated by lithiation of the *S*-aziridine stereocentre. Although we do not yet have a model to account for this sense of induction, we note that opposite stereoselectivity is observed with aziridines and epoxides. This is most apparent in the results presented in Scheme 9 where alcohol (1*S*,3a*R*,6a*R*)-**27** (generated by an epoxide rearrangement using (−)-sparteine) was converted into sulfonamide (1*S*,3a*R*,6a*R*)-**25**, enantiomeric to that generated by rearrangement of aziridine **10** using (−)-sparteine (see Scheme 8). In all of the examples reported to date from the Hodgson group,[4,5] the use of (−)-sparteine as a ligand leads to preferential lithiation of the *R*-stereocentre (to varying degrees, depending on the substrate) thus generating lithiated epoxides **33** and **34**. Clearly, the presence of a *N*-tosyl group in aziridines permits a complete changeover of the enantiodiscriminating



Scheme 10.

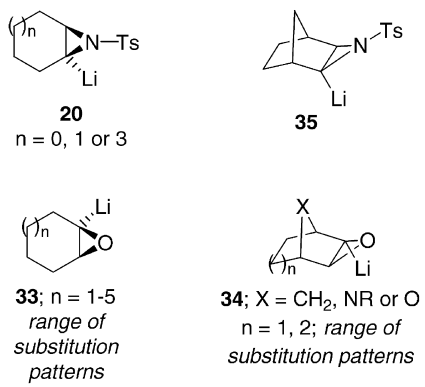


Figure 1.

interactions between the alkyllithium-(−)-sparteine complex and the substrate. With *N*-tosyl aziridines, it is conceivable that the first step in the mechanism is stereoselective complexation of the alkyllithium to the oxygen of one of the enantiotopic S=O groups and this could be the source of the reversal in stereoselectivity compared to epoxides. Two other unpublished results from Müller and co-workers[26] are also consistent with preferential lithiation of the *S*-stereocentre in *N*-tosyl aziridines using *sec*-butyllithum/(−)-sparteine.

We have also carried out a preliminary study on the scope and limitations of the rearrrangement of aziridines **7**–**10** using *sec*-butyllithium. This included replacing (−)-sparteine by TMEDA and trying the reactions in the absence of any ligand (in both THF and diethyl ether). The TMEDA reactions were carried out in the same way as the (−)-sparteine ones described previously (i.e. an aziridine solution was added to the *sec*-butyllithium/ligand solution at −78°C). However, for reactions with no ligand present, it was experimentally easier to add the *sec*-butyllithium to a solution of the aziridine at −78°C and so this procedure was adopted. The full results of this study are presented in Scheme 10 and Table 1.

Table 1. Rearrangement of *N*-tosyl aziridines using *sec*-butyllithium under different conditions[a]

Entry	SM (*n*)[b]	Ligand	Solvent	Product	Yield (%)[c]	ee (%)[d]	$TsNH_2$ (%)[e]	SM (%)[f]
1	**7** (0)	(−)-Sparteine	Et_2O	(*R*)-**17**	39	64	47	–
2	**7** (0)	TMEDA	Et_2O	*rac*-**17**	23	–	38	–
3	**7** (0)	–	Et_2O	*rac*-**17**	8	–	69	–
4	**7** (0)	–	THF	*rac*-**17**	10	–	56	–
5	**8** (1)	(−)-Sparteine	Et_2O	(*R*)-**11**	67	38	10	–
6	**8** (1)	TMEDA	Et_2O	*rac*-**11**	22	–	nd[g]	–
7	**8** (1)	–	Et_2O	*rac*-**11**	57	–	30	–
8	**8** (1)	–	THF	*rac*-**11**	4	–	56	–
9	**9** (2)	(−)-Sparteine	Et_2O	–[h]	–	–	–	–
10	**9** (2)	–	Et_2O	*rac*-**36**	23	–	31	17
11	**10** (3)	(−)-Sparteine	Et_2O	**25**	71	66	–	–
12	**10** (3)	TMEDA	Et_2O	*rac*-**25**	26	–	–	–
13	**10** (3)	–	Et_2O	*rac*-**25**	34	–	–	23
14	**10** (3)	–	THF	*rac*-**25**	36	–	–	–

[a] Conditions: 2.9 equiv. ^{s}BuLi, 2.9 equiv. ligand (if applicable), Et_2O or THF, −78°C, 4 h then rt over 1 h.
[b] Starting material.
[c] Isolated yield of product after chromatography.
[d] Enantiomeric excess determined by chiral HPLC.
[e] Isolated yield of $TsNH_2$ after chromatography.
[f] Isolated yield of recovered starting material after chromatography.
[g] Not determined.
[h] No isolable compounds (including starting material) were obtained.

As mentioned previously, rearrangement of the cycloheptene *N*-tosyl aziridine **9** using *sec*-butyllithium/(−)-sparteine generated no isolable compounds, including starting material (entry 9). In contrast, cyclopropylsulfonamide **36** (23% yield) was isolated from the analogous reaction in diethyl ether in the absence of ligand. Evidence for the formation of the cyclopropyl ring in **36** was provided by characteristic upfield resonances at δ_H 0.94–0.82, 0.46 and 0.08 ppm in the ^{1}H NMR spectrum and at δ_C 15.9 (CH), 12.5 (CH) and 8.0 (CH_2) in the ^{13}C NMR spectrum. The relative stereochemistry of **36** has not been established unequivocally. However, we assigned a *cis* relationship between the NHTs group and the cyclopropane ring based on the precedent in the corresponding cycloheptene oxide rearrangement reaction[35] and by comparing the likely conformations for C–H insertion in the cyclooctene and cycloheptene *N*-tosyl aziridines, **37** and **38**, respectively (Fig. 2).

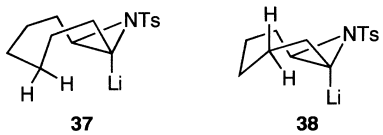


Figure 2.

Some important and interesting trends can be identified from the results presented in Table 1. Apart from the cycloheptene *N*-tosyl aziridine **9**, the highest yields of rearrangement products were obtained in the presence of (−)-sparteine (entries 1, 5, and 11). In contrast, use of TMEDA or no ligand generally led to lower product yields and an increase in the amount of $TsNH_2$ that was generated (entries 2, 3, 4, and 8). To explain this, we suggest that in the absence of the sterically hindered (−)-sparteine ligand, the lithiated aziridines are more susceptible to nucleophilic attack by a second equivalent of *sec*-butyllithium, as outlined in Scheme 6. This alternative process appears to occur more readily for the cyclopentene *N*-tosyl aziridine **7** (and also for the cyclopentene *N*-tosyl aziridine *cis*-**6**, Scheme 7). However, the reaction of cyclohexene *N*-tosyl aziridine **8** with *sec*-butyllithium in diethyl ether (entry 7) appears anomalous as a 57% isolated yield of allylic sulfonamide *rac*-**11** was obtained. In the reactions of cyclooctene *N*-tosyl aziridine **10**, we have never observed the formation of any $TsNH_2$ (entries 11–14) and the low yielding reactions in the absence of ligand (entries 12–14) are presumably due to another competing process that we have not yet identified. Finally, we note that the highest enantioselectivity was observed with the cyclooctene *N*-tosyl aziridine **10** (entry 11).

3. Conclusion

The reactions between *sec*-butyllithium and the five cycoalkene *N*-tosyl aziridines presented in this paper have allowed us to draw some important synthetic, mechanistic and stereochemical conclusions. Firstly, the predominant sense of asymmetric induction in the lithiation-rearrangement of *N*-tosyl aziridines **7**, **8** and **10** using (−)-sparteine is opposite to the corresponding epoxides: the *R*-epoxide stereocentre is lithiated preferentially but the aziridine rearrangement products (*R*)-**11**, (*R*)-**17** and (1*R*,3a*S*,6a*S*)-**25** are generated via lithiation of the *S*-aziridine stereocentre. For the cyclooctene aziridine (**10**) and epoxide (**26**), the results described in this paper provide a direct comparison as almost equal and opposite asymmetric induction are observed under near-identical conditions: aziridine **10** gave (1*R*,3a*S*,6a*S*)-**25** in 71% yield and 66% ee (Scheme 8) whereas epoxide **26** gave (1*S*,3a*R*,6a*R*)-**25** in 84% yield and 69% ee (Scheme 9) using *sec*-butyllithium/(−)-sparteine. Three other examples of *N*-tosyl aziridines rearrangement reactions, reported by Müller and co-workers,[11,26] also proceed via lithiation of the *S*-aziridine stereocentre.

Secondly, we have rationalised the formation of $TsNH_2$ (to varying degrees) in the rearrangement reactions by considering attack by a second equivalent of *sec*-butyllithium on the electrophilic lithiated aziridines. Specifically, the conversion of *N*-tosyl aziridine *cis*-**6** into alkene **24** (together with the formation of $TsNH_2$) is the first example of the reductive alkylation of lithiated aziridines and may have useful synthetic applications, as both Hodgson[5a,b,34] and Mioskowski[32,33] have demonstrated with epoxides. Thirdly, there is a significant ligand effect in the *N*-tosyl aziridine reactions and our results suggest that a ligand (e.g. (−)-sparteine or TMEDA) is not required for α-lithiation but has a key role in determining the fate of the lithiated aziridine. Hodgson et al. have recently noted dramatic ligand effects in some related epoxide reactions.[5a] The highest yields of allylic sulfonamides **11** and **17** were obtained from the reactions in the presence of sterically hindered (−)-sparteine. We suggest that the use of the less hindered TMEDA or no ligand (diethyl ether or THF presumably coordinated to the lithium) allows the alternative reductive alkylation pathway (generating alkenes and $TsNH_2$) to occur preferentially. Most of the lower yielding reactions (Table 1, entries 1–4, 8, and 10) are accompanied by higher yields of $TsNH_2$. Fourthly, reductive alkylation is most pronounced with cyclopentene *N*-tosyl aziridines *cis*-**6** and **7** compared to the cyclohexene, cycloheptene and cyclooctene analogues.

Finally, from a synthetic viewpoint, we recommend the use of a bulky diamine ligand in diethyl ether as a way of generating rearrangement products and the use of no ligand in THF or diethyl ether as a means of producing reductive alkylation products. Further work is required to fully understand these reactions. However, it is hoped that the results and conclusions presented in this paper provide a strong foundation for future developments in the synthetic utility of lithiated aziridines generated by direct α-lithiation/deprotonation.

4. Experimental

4.1. General

Water is distilled water. Et_2O and THF were freshly distilled from sodium benzophenone ketyl whereas CH_2Cl_2 was freshly distilled from calcium hydride. All non-aqueous reactions were carried out under oxygen-free nitrogen using oven-dried glassware. Petrol refers to the fraction of petroleum ether boiling in the range 40–60°C. Brine refers to a saturated aqueous solution of NaCl.

Flash column chromatography was carried out using ICN Biomedicals GmbH silica (60 Å) or Fisher Matrex silica 60, 70–200 μm. Thin layer chromatography was carried out using commercially available Merck F_{254} aluminium-backed silica plates. Proton (270 or 400 MHz) and carbon (67.9 or 100.6 MHz) NMR spectra were recorded on a Jeol EX-270 or a Jeol ECX-400 instrument using an internal deuterium lock. All samples were recorded as solutions in $CDCl_3$ and chemical shifts are quoted in parts per million downfield of tetramethylsilane. Carbon NMR spectra were recorded with broad band proton decoupling and were assigned using DEPT experiments. Melting points were measured on a Gallenkamp melting point apparatus and are uncorrected. Infrared spectra were recorded on an ATI Matteson Genesis FT-IR spectrometer. Chemical ionisation and high resolution mass spectra were recorded on a Fisons Analytical (VG) Autospec spectrometer. Optical rotations were recorded at 20°C on a Jasco DIP-370 polarimeter (using the sodium D line; 589 nm) and $[\alpha]_D$ are given in 10^{-1} deg cm^2 g^{-1}. Microanalyses were carried out at the University of Newcastle on a Carlo Erba 1106 elemental analyser and weighed using a Mettler MT 5 microbalance.

n-Butyllithium and *sec*-butyllithium were titrated against *N*-benzylbenzamide before use.[36] (−)-Sparteine, TMEDA and (1*R*,2*S*)-*N*-methyl-1-phenyl-2-(1-pyrrolidinyl)-1-propanamine were purified by Kugelrohr distillation immediately prior to use. 3-Cyclopenten-1-ol is commercially available from Astatech Inc., Philadelphia (USA). (1*R*,2*S*)-*N*-Methyl-1-phenyl-2-(1-pyrrolidinyl)-1-propanamine[28b] and TsNHBoc[37] were prepared according to the literature procedures.

4.1.1. General procedure A: preparation of *N*-tosyl aziridines. $PhMe_3N^+Br_3^-$ (0.1 equiv.) was added to a stirred solution of alkene (0.16 mmol) and Chloramine-T (1.1 equiv.) in MeCN (2 mL) at rt under N_2. After stirring for 16 h at rt, the reaction mixture was filtered through a plug of silica and washed well with Et_2O. Then, the filtrate was evaporated under reduced pressure to give the crude product.

4.1.2. General procedure B: rearrangement of aziridines using *sec*-butyllithium/diamine. *sec*-Butyllithium (2.9 equiv. of 1.2 M solution in cyclohexane) was added dropwise to a stirred solution of (−)-sparteine or TMEDA (2.9 equiv.) in Et_2O (3 mL) at −78 °C under N_2. After stirring for 15 min, a solution of aziridine (0.5 mmol) in Et_2O (2 mL) was added dropwise via cannula. After stirring for 4 h at −78 °C, the solution was allowed to warm to rt and saturated $NH_4Cl_{(aq)}$ (10 mL) was added. The layers were separated and the aqueous layer was extracted with Et_2O (3×10 mL). The combined Et_2O extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product.

4.1.3. General procedure C: rearrangement of aziridines using *sec*-butyllithium. *sec*-Butyllithium (2.9 equiv. of 1.2 M solution in cyclohexane) was added dropwise to a stirred solution of aziridine (0.5 mmol) in Et_2O or THF (5 mL) at −78°C under N_2. After stirring for 4 h at −78°C, the solution was allowed to warm to rt and saturated $NH_4Cl_{(aq)}$ (10 mL) was added. The layers were separated and the aqueous layer was extracted with Et_2O (3×10 mL). The combined Et_2O extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product.

4.2. *tert*-Butyl(diphenyl)silyl 3-cyclopenten-1-yl ether 5

Imidazole (404 mg, 5.9 mmol) and *tert*-butyldiphenylsilyl chloride (654 mg, 2.4 mmol) were added in portions to a stirred solution of 3-cyclopenten-1-ol (200 mg, 2.4 mmol) in CH_2Cl_2 (6 mL) at rt under nitrogen. After stirring for 16 h, water (5 mL) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3×5 mL) and the combined CH_2Cl_2 extracts were washed with brine (10 mL), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol–Et_2O (95:5) as eluent gave alkene **5** (768 mg, 100%) as a cloudy oil, R_F(99:1 petrol–Et_2O) 0.6; IR (CH_2Cl_2) 3072, 2933, 2858, 1427, 1109 cm^{-1}; ^1H NMR (270 MHz; $CDCl_3$) 7.70–7.68 (m, 4H), 7.47–7.36 (m, 6H), 5.63 (br s, 2H), 4.61–4.53 (m, 1H), 2.44–2.40 (m, 4H), 1.07 (s, 9H); ^{13}C NMR (67.9 MHz; $CDCl_3$) 135.7, 134.5, 129.5, 128.3, 127.5, 73.5, 42.4, 26.9, 19.1; MS (CI, NH_3) 323 $(M+H)^+$, 282, 265, 216, 199; HRMS (CI, NH_3) *m/z* calcd for $C_{21}H_{26}OSi$ $(M+H)^+$ 323.1831, found 323.1833.

4.3. 3-{[*tert*-Butyl(diphenyl)silyl]oxy}-6-[(4-methylphenyl)sulfonyl]-6-azabicyclo[3.1.0]hexane *trans*-6 and *cis*-6

Using general procedure A, alkene **5** (500 mg, 1.55 mmol), Chloramine-T trihydrate (480 mg, 1.70 mmol) and $PhMe_3N^+Br_3^-$ (60 mg, 0.16 mmol) in MeCN (20 mL) gave the crude product which contained a 37:63 mixture of aziridines *trans*-**6** and *cis*-**6** (by ^1H NMR spectroscopy). Purification by flash chromatography on silica with petrol–Et_2O (7:3) as eluent gave aziridine *trans*-**6** (271 mg, 36%) as a white solid, mp 118–119°C (from EtOAc); R_F(7:3 petrol–Et_2O) 0.3; IR ($CDCl_3$) 3072, 3052, 2962, 1429, 1159, 1090, 758, 652 cm^{-1}; ^1H NMR (270 MHz; $CDCl_3$) 7.70 (br d, 2H, *J*=8.5 Hz), 7.63–7.58 (m, 4H), 7.48–7.28 (m, 8H), 4.12 (quin., 1H, *J*=7.5 Hz), 3.29 (br s, 2H), 2.43 (s, 3H), 2.18 (dd, 2H, *J*=7.5, 14.0 Hz), 1.76 (dddd, 2H, *J*=0.5, 1.5, 7.5, 14.0 Hz), 1.01 (s, 9H); ^{13}C NMR (67.9 MHz; $CDCl_3$) 144.1, 135.6, 135.4, 133.6, 129.7, 129.6, 127.62, 127.58, 70.7, 45.0, 36.3, 26.8, 21.6, 18.9; MS (CI, NH_3) 492 $(M+H)^+$, 434, 338, 216, 196, 82; HRMS (CI, NH_3) *m/z* calcd for $C_{28}H_{33}NO_3SiS$ $(M+H)^+$ 492.2029, found 492.2023. Anal. calcd for $C_{28}H_{33}NO_3SiS$: C, 68.39; H, 6.76; N, 2.85; found: C, 67.5; H, 6.9; N, 2.5 and aziridine *cis*-**6** (378 mg, 50%) as a white solid, mp 89–90°C (from EtOAc); R_F(7:3 petrol–Et_2O) 0.2; IR ($CDCl_3$) 3695, 3072, 3053, 2960, 2931, 2860, 2260, 1159, 1093 cm^{-1}; ^1H NMR (270 MHz; $CDCl_3$) 7.94 (br d, 2H, *J*=8.5 Hz), 7.64–7.59 (m, 4H), 7.46–7.31 (m, 8H), 4.36 (br t, 1H, *J*=6.5 Hz), 3.36 (br s, 2H), 2.47 (s, 3H), 2.03 (dd, 2H *J*=1.0, 15.0 Hz), 1.89 (br dd, 2H, *J*=6.5, 15.0 Hz), 1.03 (s, 9H); ^{13}C NMR (67.9 MHz; $CDCl_3$) 143.9, 136.4, 135.8, 134.0, 129.5, 129.4, 127.6, 127.5, 72.7, 46.3, 37.9, 26.7, 21.6, 19.0; MS (CI, NH_3) 492 $(M+H)^+$, 434, 338, 216, 196, 82; HRMS (CI, NH_3) *m/z* calcd for $C_{28}H_{33}NO_3SiS$ $(M+H)^+$ 492.2029, found 492.2021. Anal. calcd for $C_{28}H_{33}NO_3SiS$: C, 68.39; H, 6.76; N, 2.85; found: C, 68.1; H, 6.9; N, 2.6.

4.4. 6-[(4-Methylphenyl)sulfonyl]-6-azabicyclo[3.1.0]-hexane 7

Using general procedure A, cyclopentene (500 mg, 7.34 mmol), Chloramine-T trihydrate (2.3 g, 8.1 mmol) and $PhMe_3N^+Br_3^-$ (276 mg, 0.73 mmol) in MeCN (30 mL) gave the crude product. Purification by flash chromatography on silica with petrol–EtOAc (9:1) as eluent gave aziridine **7** (1.54 g, 88%) as a white solid, mp 71–72°C (lit.,[25] 71–72°C). Spectroscopic data identical to that reported in the literature.[18a,25]

4.5. 7-[(4-Methylphenyl)sulfonyl]-7-azabicyclo[4.1.0]-heptane 8

Using general procedure A, cyclohexene (500 mg, 6.1 mmol), Chloramine-T trihydrate (1.89 g, 6.7 mmol) and $PhMe_3N^+Br_3^-$ (229 mg, 0.61 mmol) in MeCN (30 mL) gave the crude product. Purification by flash chromatography on silica with petrol–EtOAc (9:1) as eluent gave aziridine **8** (1.13 g, 74%) as a white solid, mp 55–56°C (lit.,[23a] 55–56°C). Spectroscopic data identical to that reported in the literature.[23a]

4.6. 8-[(4-Methylphenyl)sulfonyl]-8-azabicyclo[5.1.0]-octane 9

Using general procedure A, cycloheptene (500 mg, 5.2 mmol), Chloramine-T trihydrate (1.61 g, 5.3 mmol) and $PhMe_3N^+Br_3^-$ (195 mg, 0.52 mmol) in MeCN (30 mL) gave the crude product. Purification by flash chromatography on silica with petrol–EtOAc (9:1) as eluent gave aziridine **9** (870 mg, 63%) as a white solid, mp 75–76°C; R_F(1:1 petrol–Et_2O) 0.4; IR ($CHCl_3$) 3060, 2958, 2879, 1421, 1401, 1318, 1248, 1155, 1090 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 7.82 (br d, 2H, J=8.5 Hz), 7.32 (br d, 2H, J=8.5 Hz), 3.00–2.89 (m, 2H), 2.45 (s, 3H), 1.94–1.73 (m, 4H), 1.64–1.37 (m, 6H); ^{13}C NMR (67.9 MHz, $CDCl_3$) 143.8, 135.7, 129.4, 127.3, 44.1, 30.8, 27.9, 25.0, 21.4; MS (CI, NH_3) 266 $(M+H)^+$; HRMS (CI, NH_3) *m/z* calcd for $C_{14}H_{19}NO_2S$ $(M+H)^+$ 266.1215, found 266.1214.

4.7. 9-[(4-Methylphenyl)sulfonyl]-9-azabicyclo[6.1.0]-nonane 10

Using general procedure A, *cis*-cyclooctene (3.00 g, 27.2 mmol), Chloramine-T trihydrate (8.44 g, 29.9 mmol) and $PhMe_3N^+Br_3^-$ (1.02 g, 2.7 mmol) in MeCN (150 mL) gave the crude product. Purification by flash chromatography on silica with petrol–EtOAc (9:1) as eluent and then recrystallisation from petrol–EtOAc gave aziridine **10** (1.50 g, 20%) as white needles, mp 124–125°C (lit.,[38] 125°C). Spectroscopic data identical to that reported in the literature.[39]

4.8. *N*-[(1*R*)-2-Cyclohexen-1-yl]-4-methylbenzene-sulfonamide (*R*)-11

Using general procedure B, aziridine **8** (126 mg, 0.5 mmol), *sec*-butyllithium (1.19 mL of a 1.2 M solution in cyclohexane, 1.45 mmol) and (−)-sparteine (333 μL, 1.45 mmol) in Et_2O (5 mL) gave the crude product. Purification by flash chromatography on silica with pentane–EtOAc (8:2) as eluent gave allylic sulfonamide (*R*)-**11** (85 mg, 67%, 38% ee by chiral HPLC) as a white solid, mp 99–100°C (lit.,[11] 104–106°C); $[\alpha]_D$= +27.8 (*c* 1.0 in $CHCl_3$)(lit.,[11] $[\alpha]_D$=+19.8 (*c* 1.5 in $CHCl_3$) for 39% ee); HPLC: Chiralcel AD-H, pentane–EtOH–TFA (75:25:0.1), 1.0 mL min^{-1}, 230 nm, 12.5 min [(*R*)-**11**], 14.6 [(*S*)-**11**] and $TsNH_2$ (9 mg, 10%) as a white solid. Spectroscopic data of (*R*)-**11** identical to that reported in the literature.[11,18a]

4.9. (1*S*)-2-Cyclohexen-1-ol (*S*)-14

n-Butyllithium (9.4 mL of a 2.2 M solution in hexanes, 20.4 mmol) was added dropwise to a stirred solution of (1*R*,2*S*)-*N*-methyl-1-phenyl-2-(1-pyrrolidinyl)-1-propanamine[28b] (4.39 g, 20.4 mmol) in THF (100 mL) at 0°C under N_2. After stirring for 30 min at 0°C, cyclohexene oxide **13** (1.00 g, 10.2 mmol) was added dropwise and the resulting solution was allowed to warm to rt. After stirring for 16 h at rt, saturated $NH_4Cl_{(aq)}$ (60 mL) was added and the layers were separated. The aqueous layer was extracted with Et_2O (3×50 mL) and the combined Et_2O extracts were washed with 2 M $HCl_{(aq)}$ (2×50 mL), dried (Na_2SO_4) and evaporated under reduced pressure (water bath <40°C) to give the crude product. Purification by distillation gave alcohol (*S*)-**14** (370 mg, 37, 81% ee by Mosher's ester formation) as a colourless liquid, bp 62–63°C/15 mm Hg(lit.,[40] 75–76°C/23 mm Hg); $[\alpha]_D$=−132.9 (*c* 1.0 in $CHCl_3$)(lit.,[41] $[\alpha]_D$=+130.6 (*c* 1.21 in $CHCl_3$) for (*R*)-**14** of 99% ee). Spectroscopic data identical to that reported in the literature.[42]

4.10. *N*-[(1*R*)-2-Cyclohexen-1-yl]-4-methylbenzene-sulfonamide (*R*)-11

DEAD (404 μL, 2.56 mmol) was added dropwise to a stirred solution of alcohol (*S*)-**14** (100 mg, 1.20 mmol, 81% ee), PPh_3 (801 mg, 3.06 mmol) and TsNHBoc[38] (446 mg, 1.53 mmol) in THF (3 mL) at rt under N_2. After stirring for 10 h at rt, the solvent was evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol–EtOAc (8:2) as eluent gave Boc protected allylic sulfonamide (*R*)-**15** (340 mg, 95%) as an off-white solid. Spectroscopic data identical to that described below.

TFA (263 μL, 3.41 mmol) was added dropwise to a stirred solution of Boc protected allylic sulfonamide (*R*)-**15** (100 mg, 0.29 mmol) in CH_2Cl_2 (1 mL) at 0°C under N_2. The resulting solution was allowed to warm to rt. After stirring for 1 h at rt, 5% $NaHCO_{3(aq)}$ (5 mL) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2×5 mL) and the combined CH_2Cl_2 extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol–EtOAc (8:2) as eluent gave allylic sulfonamide (*R*)-**11** (36 mg, 50%, 18% ee by chiral HPLC) as a white solid, $[\alpha]_D$=+11.6 (*c* 1.0 in $CHCl_3$); HPLC: Chiralcel AD-H, pentane–EtOH–TFA (75:25:0.1), 1.0 mL min^{-1}, 230 nm, 12.3 min [(*R*)-**11**], 14.4 [(*S*)-**11**]. Spectroscopic data identical to that reported in the literature.[11,18a]

4.11. *tert*-Butyl 2-cyclohexen-1-yl[(4-methylphenyl)-sulfonyl]carbamate (*R*)-15

A solution of di-*tert*-butyl dicarbonate (100 mg, 0.46 mmol) in CH_2Cl_2 (0.8 mL) was added dropwise to a stirred solution of allylic sulfonamide (*R*)-**11** (100 mg, 0.4 mmol, 38% ee), Et_3N (61 μL, 0.44 mmol) and DMAP (5 mg, 40 μmol) in CH_2Cl_2 (0.5 mL) at rt under nitrogen. After stirring for 16 h at rt, the solvent was evaporated under reduced pressure. EtOAc (2.5 mL) and 20% $HCl_{(aq)}$ (5 mL) were added and the layers were separated. The organic layer was washed with water (5 mL) and brine (5 mL), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol–EtOAc (8:2) as eluent gave Boc-protected allylic sulfonamide (*R*)-**15** (122 mg, 87, 38% ee assumed) as a white solid, mp 91–92°C (from EtOAc); R_F(8:2 petrol–EtOAc) 0.7; $[\alpha]_D$=+10.7 (*c* 1.0 in $CHCl_3$); IR (CH_2Cl_2) 3061, 2983, 2939, 2868, 1727, 1354, 1245, 1153 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 7.82 (br d, 2H, *J*=8.5 Hz), 7.31 (br d, 2H, *J*=8.5 Hz), 5.80–5.70 (m, 1H), 5.51 (br d, 1H, *J*=10.0 Hz), 5.16–5.05 (m, 1H), 2.44 (s, 3H), 2.30–1.65 (m, 6H), 1.35 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) 150.5, 143.8, 137.7, 129.2, 128.7, 128.2, 127.6, 83.9, 56.2, 28.3, 27.8, 23.9, 22.5, 21.5; MS (CI, NH_3) 369 $(M+NH_4)^+$, 313, 269; HRMS (CI, NH_3) *m/z* calcd for $C_{18}H_{25}NO_4S$ $(M+NH_4)^+$ 369.1848, found 369.1851.

4.12. *tert*-Butyl (1*R*)-2-cyclohexen-1-ylcarbamate (*R*)-16

A solution of Boc-protected allylic sulfonamide (*R*)-**15** (122 mg, 0.35 mmol) in THF (4 mL) was added dropwise to a stirred solution of sodium (80 mg, 3.47 mmol) in ammonia (approx. 20 mL) at −78°C under N_2. After stirring for 1 h at −78°C, the solution was allowed to warm to rt and stirred at rt for 1 h. Then, the solvent was allowed to evaporate by removing the cold-trap condenser. Saturated $NH_4Cl_{(aq)}$ (10 mL) and EtOAc (10 mL) were added and the layers were separated. The organic layer was washed with 0.1 M $NaOH_{(aq)}$ (2×10 mL) and brine (10 mL), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol–EtOAc (9:1) as eluent gave carbamate (*R*)-**16** (35 mg, 51%, 38% ee assumed) as a white solid, mp 52–53°C (lit.,[17] 48°C); R_F(9:1 petrol–EtOAc) 0.3; $[\alpha]_D$=+30.0 (*c* 1.1 in $CHCl_3$)(lit.,[17] $[\alpha]_D$=+101 (*c* 2.8 in $CHCl_3$) for (*R*)-**16** of 95% ee). Spectroscopic data identical to that reported in the literature.[17]

4.13. *N*-[(1*R*)-2-Cyclopenten-1-yl]-4-methylbenzene-sulfonamide (*R*)-17

Using general procedure B, aziridine **7** (119 mg, 0.5 mmol), *sec*-butyllithium (1.19 mL of a 1.2 M solution in cyclohexane, 1.45 mmol) and (−)-sparteine (333 μL, 1.45 mmol) in Et_2O (5 mL) gave the crude product. Purification by flash chromatography on silica with pentane–EtOAc (8:2) as eluent gave allylic sulfonamide (*R*)-**17** (46 mg, 39%, 64% ee by chiral HPLC) as a white solid, mp 73–74°C; $[\alpha]_D$=+15.4 (*c* 1.0 in $CHCl_3$); HPLC: Chiralcel OJ-R, hexane–^{i}PrOH (9:1), 1.0 mL min^{-1}, 230 nm, 7.3 min [(*S*)-**17**], 7.6 [(*R*)-**17**] and $TsNH_2$ (40 mg, 47%) as a white solid. Spectroscopic data of (*R*)-**17** identical to that reported in the literature.[18a,43]

4.14. *tert*-Butyl (1*R*)-2-cyclopenten-1-yl[(4-methyl-phenyl)sulfonyl]carbamate (*R*)-18

A solution of di-*tert*-butyl dicarbonate (185 mg, 0.85 mmol) in CH_2Cl_2 (2 mL) was added dropwise to a stirred solution of allylic sulfonamide (*R*)-**17** (175 mg, 0.74 mmol, 64% ee), Et_3N (113 μL, 0.81 mmol) and DMAP (9 mg, 73 μmol) in CH_2Cl_2 (1 mL) at rt under nitrogen. After stirring for 16 h at rt, the solvent was evaporated under reduced pressure. EtOAc (5 mL) and 20% $HCl_{(aq)}$ (10 mL) were added and the layers were separated. The organic layer was washed with water (10 mL) and brine (10 mL), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol–EtOAc (8:2) as eluent gave Boc-protected allylic sulfonamide (*R*)-**18** (172 mg, 69, 64% ee assumed) as a white solid, mp 85–86°C (from Et_2O); R_F(8:2 petrol–EtOAc) 0.4; $[\alpha]_D$=+51.2 (*c* 1.0 in $CHCl_3$); IR ($CHCl_3$) 3022, 2983, 1724, 1352, 1151 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 7.82 (br d, 2H, *J*=8.5 Hz), 7.33 (br d, 2H, *J*=8.5 Hz), 5.95–5.84 (m, 1H), 5.69–5.55 (m, 2H), 5.16–5.05 (m, 1H), 2.71–2.53 (m, 1H), 2.48–2.26 (m, 2H), 2.44 (s, 3H), 2.16–1.92 (m, 1H), 1.32 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) 150.6, 143.8, 137.9, 133.0, 129.7, 129.2, 127.6, 84.0, 64.6, 31.7, 28.7, 27.8, 21.6; MS (CI, NH_3) 355 $(M+NH_4)^+$, 338, 299; HRMS (CI, NH_3) *m/z* calcd for $C_{17}H_{23}NO_4S$ $(M+NH_4)^+$ 355.1692, found 355.1693.

4.15. *tert*-Butyl (1*R*)-2-cyclopenten-1-ylcarbamate (*R*)-19

A solution of Boc-protected allylic sulfonamide (*R*)-**18** (130 mg, 0.39 mmol) in THF (4 mL) was added dropwise to a stirred solution of sodium (89 mg, 3.85 mmol) in ammonia (approx. 20 mL) at −78°C under N_2. After stirring for 1 h at −78°C, the solution was allowed to warm to rt and stirred at rt for 1 h. Then, the solvent was allowed to evaporate by removing the cold-trap condenser. Saturated $NH_4Cl_{(aq)}$ (10 mL) and EtOAc (10 mL) were added and the layers were separated. The organic layer was washed with 0.1 M $NaOH_{(aq)}$ (2×10 mL) and brine (10 mL), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol–EtOAc (9:1) as eluent gave carbamate (*R*)-**19** (50 mg, 69, 64% ee assumed) as a white solid, mp 86–87°C (lit.,[17] 87.5°C); R_F(9:1 petrol–EtOAc) 0.2; $[\alpha]_D$=+38.8 (*c* 1.0 in CH_2Cl_2)(lit.,[17] $[\alpha]_D$=+77.0 (*c* 5.1 in CH_2Cl_2) for (*R*)-**19** of 87% ee). Spectroscopic data identical to that reported in the literature.[17]

4.16. 3-*sec*-Butyl-3-cyclopenten-1-yl *tert*-butyl-(diphenyl)silyl ether 24

Using general procedure C, aziridine *cis*-**6** (246 mg, 0.5 mmol) and *sec*-butyllithium (1.16 mL of a 1.25 M solution in cyclohexane, 1.45 mmol) in Et_2O (2.5 mL) gave the crude product. Purification by flash chromatography on silica with pentane–Et_2O (7:3) as eluent gave a 50:50 mixture (by ^1H NMR spectroscopy) of diastereomeric alkenes **24** (143 mg, 76%) as a colourless oil, R_F(7:3

petrol–Et_2O) 0.65; IR (CH_2Cl_2) 3072, 2962, 2931, 2860, 1462, 1427, 1365, 1109 cm^{-1}; ^1H NMR (270 MHz; $CDCl_3$) 7.74–7.68 (m, 4H), 7.47–7.36 (m, 6H), 5.21 (br s, 1H), 4.58–4.50 (m, 1H), 2.47–2.42 (m, 2H), 2.13 and 2.11 (sextet, 1H, J=6.5 Hz), 1.47–1.23 (m, 2H), 1.08 (s, 9H), 1.00 and 0.98 (d, 3H, J=6.5 Hz), 0.85 and 0.81 (t, 3H, J=6.5 Hz); ^{13}C NMR (67.9 MHz; $CDCl_3$) 146.8 and 146.7, 135.73 and 135.71, 134.63 and 134.60, 129.4, 127.5, 119.8 and 119.7, 73.9 and 73.8, 42.1 and 42.0, 41.9 and 41.8, 37.0 and 36.8, 27.8 and 27.7, 26.9, 19.1 and 18.9, 18.5, 11.8 and 11.5 (some diastereomeric signals not resolvable); MS (CI, NH_3) 379 $(M+H)^+$, 123; HRMS (CI, NH_3) m/z calcd for $C_{25}H_{34}OSi$ $(M+H)^+$ 379.2457, found 379.2460.

4.17. 3-*sec*-Butyl-3-cyclopenten-1-yl *tert*-butyl-(diphenyl)silyl ether 24

Using general procedure C, aziridine *cis*-**6** (246 mg, 0.5 mmol) and *sec*-butyllithium (1.16 mL of a 1.25 M solution in cyclohexane, 1.45 mmol) in THF (2.5 mL) gave the crude product. Purification by flash chromatography on silica with pentane–Et_2O (7:3) as eluent gave alkene **24** (133 mg, 70%) as a colourless oil. Spectroscopic data identical to that described above.

4.18. *N*-[(1*R*,3a*S*,6a*S*)-Octahydro-1-pentalenyl]-4-methylbenzenesulfonamide (1*R*,3a*S*,6a*S*)-25

Using general procedure B, aziridine **10** (126 mg, 0.5 mmol), *sec*-butyllithium (1.19 mL of a 1.25 M solution in cyclohexane, 1.45 mmol) and (−)-sparteine (333 μL, 1.45 mmol) in Et_2O (5 mL) gave the crude product. Purification by flash chromatography on silica with pentane–EtOAc (8:2) as eluent gave bicyclic sulfonamide (1*R*,3a*S*,6a*S*)-**25** (100 mg, 71%, 66% ee by chiral HPLC) as a white solid, mp 109–110°C (lit.,[11] 106–108°C); $[\alpha]_D$=+21.2 (c 1.0 in $CHCl_3$)(lit.,[11] $[\alpha]_D$=+29.1 (c 1.0 in $CHCl_3$) for 75% ee); HPLC: Chiralcel OD, hexane–^{i}PrOH (96:4), 1.0 mL min^{-1}, 230 nm, 28.5 min [(1*S*,3a*R*,6a*R*)-**25**], 30.7 [(1*R*,3a*S*,6a*S*)-**25**]. Spectroscopic data identical to that reported in the literature.[11,18a]

4.19. (1*S*,3a*R*,6a*R*)-Octahydro-1-pentalenol (1*S*,3a*R*,6a*R*)-27

sec-Butyllithium (15 mL of 1.3 M solution in cyclohexane, 19.0 mmol) was added dropwise to a stirred solution of (−)-sparteine (4.4 mL, 19.0 mmol) in Et_2O (40 mL) at −78°C under N_2. After stirring for 30 min at −78°C, a solution of cyclooctene oxide **26** (1.0 g, 7.9 mmol) in Et_2O (20 mL) was added dropwise via cannula. After stirring for 5 h at −78°C, the solution was allowed to warm to rt over 1 h and stirred at rt for 16 h. 2 M $HCl_{(aq)}$ (40 mL) was added, the layers were separated and the aqueous layer was extracted with Et_2O (3×40 mL). The combined Et_2O extracts were washed with saturated $NaHCO_{3(aq)}$ (40 mL) and brine (40 mL), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica using petrol–Et_2O (1:1) as eluent gave alcohol (1*S*,3a*R*, 6a*R*)-**27** (837 mg, 84, 69% ee by chiral HPLC of the 2,4-dinitrobenzoate[4]) as a colourless oil, R_F(1:1 petrol–Et_2O) 0.4. Spectroscopic data identical to that reported in the literature.[4]

4.20. (1*R*,3a*R*,6a*R*)-Octahydro-1-pentalenyl 2,4-dinitrobenzoate (1*R*,3a*R*,6a*R*)-28

DEAD (1.47 mL of 85% purity reagent, 7.9 mmol) was added dropwise to a stirred solution of alcohol (1*S*,3a*R*,6a*R*)-**27** (400 mg, 3.2 mmol, 69% ee), PPh_3 (2.49 g, 9.5 mmol) and 2,4-dinitrobenzoic acid (1.01 g, 4.75 mmol) in THF (10.5 mL) at rt under N_2. After stirring for 64 h at rt, the solvent was evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol–Et_2O (9:1) as eluent gave 2,4-dinitrobenzoate ester **28** (687 mg, 67%) as an off-white solid, mp 57–58°C (from Et_2O); R_F(9:1 petrol–Et_2O) 0.2; $[\alpha]_D$=−15.3 (c 1.0 in $CHCl_3$); IR (CH_2Cl_2) 3105, 3040, 2954, 2866, 1733, 1549, 1350, 1288, 766 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 8.76 (d, 1H, J=2.0 Hz), 8.53 (dd, 1H, J=2.0, 8.5 Hz), 7.96 (d, 1H, J=8.5 Hz), 5.17–5.11 (m, 1H), 2.69–2.47 (m, 2H), 2.01–1.74 (m, 4H), 1.69–1.14 (m, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) 163.2, 148.8, 148.3, 133.3, 131.4, 127.3, 119.4, 86.2, 49.4, 41.8, 34.2, 31.5, 30.8, 30.4, 26.8; MS (CI, NH_3) 338 $(M+NH_4)^+$; HRMS (CI, NH_3) m/z calcd for $C_{15}H_{16}N_2O_6$ $(M+NH_4)^+$ 338.1352, found 388.1357.

4.21. (1*R*,3a*R*,6a*R*)-Octahydro-1-pentalenol (1*R*,3a*R*,6a*R*)-29

1 M $KOH_{(aq)}$ (3 mL, 3.0 mmol) was added dropwise to a stirred solution of 2,4-dinitrobenzoate ester **28** (637 mg, 2.0 mmol) in THF (5 mL) and MeOH (2 mL) at 0°C. After stirring for 30 min at 0°C, the mixture was allowed to warm to rt and Et_2O (15 mL) was added. The layers were separated and the aqueous layer was extracted with Et_2O (2×15 mL). The combined Et_2O extracts were washed with water (20 mL) and brine (20 mL), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica using petrol–Et_2O (1:1) as eluent gave alcohol **29** (208 mg, 83%) as a pale yellow oil, R_F(1:1 petrol–Et_2O) 0.2; $[\alpha]_D$=−11.9 (c 0.3 in $CHCl_3$); IR (CH_2Cl_2) 3614, 2953, 2864, 1450, 924, 758 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 3.90–3.85 (m, 1H), 2.66–2.50 (m, 1H), 2.30–2.17 (m, 1H), 2.04–1.88 (m, 1H), 1.83–1.63 (m, 4H), 1.60–1.34 (m, 3H), 1.30–1.10 (m, 3H); ^{13}C NMR (67.9 MHz, $CDCl_3$) 80.1, 52.6, 41.7, 34.3, 34.1, 31.5, 30.2, 26.5.

4.22. *tert*-Butyl (1*S*,3a*R*,6a*R*)-octahydro-1-pentalenyl-[(4-methylphenyl)sulfonyl]carbamate (1*S*,3a*R*,6a*R*)-30

DEAD (620 μL of 85% purity reagent, 3.37 mmol) was added dropwise to a stirred solution of alcohol **29** (170 mg, 1.35 mmol), PPh_3 (1.06 g, 4.04 mmol) and TsNHBoc[38] (548 mg, 2.02 mmol) in THF (4 mL) at rt under N_2. After stirring for 64 h at rt, the solvent was evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol–Et_2O (7:3) as eluent gave Boc protected bicyclic sulfonamide **30** (83 mg, 16%) as a colourless oil, R_F(7:3 petrol–Et_2O) 0.4; $[\alpha]_D$=−15.0 (c 1.0 in $CHCl_3$); IR ($CDCl_3$) 2953, 2867, 1722, 1369 1155, 924 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) 7.79 (br d, 2H, J=8.5 Hz), 7.30 (br d, 2H, J=8.5 Hz), 4.46 (ddd, 1H, J=6.0, 8.0, 12.0 Hz), 2.76 (quin., 1H, J=8.0 Hz), 2.60–2.37 (m, 2H), 2.44 (s, 3H), 1.97–1.84 (m, 1H), 1.80–1.55 (m,

5H), 1.53–1.10 (m, 3H), 1.35 (s, 9H); ^{13}C NMR (67.9 MHz, $CDCl_3$) 151.6, 143.6, 138.2, 129.1, 127.5, 83.9, 63.2, 46.5, 41.1, 35.4, 29.6, 28.3, 27.8, 27.4, 27.1, 21.5; MS (CI, NH_3) 397 $(M+NH_4)^+$, 341, 297; HRMS (CI, NH_3) *m/z* calcd for $C_{20}H_{29}NO_4S$ $(M+NH_4)^+$ 397.2161, found 397.2163.

4.23. *N*-[(1*S*,3a*R*,6a*R*)-Octahydro-1-pentalenyl]-4-methylbenzenesulfonamide (1*S*,3a*R*,6a*R*)-25

TFA (207 μL, 2.62 mmol) was added dropwise to a stirred solution of Boc protected bicyclic sulfonamide **30** (83 mg, 0.22 mmol) in CH_2Cl_2 (1 mL) at 0°C under N_2. The resulting solution was allowed to warm to rt. After stirring for 2.5 h at rt, the solvent was evaporated under reduced pressure. Excess TFA was removed by azeotroping with $CHCl_3$ (4×5 mL) to give the crude product. Purification by flash chromatography on silica with petrol–Et_2O (1:1) as eluent gave bicyclic sulfonamide (1*S*,3a*R*,6a*R*)-**25** (41 mg, 67, 70% ee by chiral HPLC) as a white solid, $[\alpha]_D=-26.5$ (*c* 1.0 in $CHCl_3$)(lit.,[11] $[\alpha]_D=+29.1$ (*c* 1.0 in $CHCl_3$) for 75% ee); HPLC: Chiralcel OD, hexane–^{i}PrOH (96:4), 1.0 mL min^{-1}, 230 nm, 28.5 min [(1*S*,3a*R*,6a*R*)-**25**], 30.7 [(1*R*,3a*S*,6a*S*)-**25**]. Spectroscopic data identical to that reported in the literature.[11,18a]

4.24. *tert*-Butyl (1*R*,3a*R*,6a*R*)-octahydro-1-pentalenyl-[(4-methylphenyl)sulfonyl]carbamate (1*R*,3a*R*,6a*R*)-31

DEAD (370 μL of 85% purity reagent, 1.98 mmol) was added dropwise to a stirred solution of alcohol (1*S*,3a*R*, 6a*R*)-**27** (100 mg, 0.79 mmol, 69% ee), PPh_3 (624 mg, 2.38 mmol) and TsNHBoc[38] (322 mg, 1.19 mmol) in THF (2.3 mL) at rt under N_2. After stirring for 64 h at rt, the solvent was evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with petrol–Et_2O (8:2) as eluent gave Boc protected bicyclic sulfonamide **31** (149 mg, 50%) as a white solid, mp 88–89°C (from Et_2O), R_F(8:2 petrol–Et_2O) 0.5; $[\alpha]_D=-30.2$ (*c* 1.0 in $CHCl_3$); IR ($CDCl_3$) 2951, 2866, 1720, 1350 1153 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) 7.77 (br d, 2H, *J*=8.0 Hz), 7.29 (br d, 2H, *J*=8.0 Hz), 4.42–4.29 (m, 1H), 2.96–2.80 (m, 1H), 2.70–2.52 (m, 1H), 2.43 (s, 3H), 2.35–2.15 (m, 1H), 2.03–1.79 (m, 2H), 1.72–1.48 (m, 5H), 1.44–1.24 (m, 1H), 1.33 (s, 9H), 1.20–1.00 (m, 1H); ^{13}C NMR (67.9 MHz, $CDCl_3$) 150.6, 143.6, 138.1, 129.2, 127.5, 84.0, 65.6, 45.6, 42.2, 33.0, 31.5, 31.3, 31.0, 27.9, 24.8, 21.5; MS (CI, NH_3) 397 $(M+NH_4)^+$, 380 $(M+H)^+$, 280; HRMS (CI, NH_3) *m/z* calcd for $C_{20}H_{29}NO_4S$ $(M+H)^+$ 380.1896, found 380.1893.

4.25. *N*-[(1*R*,3a*R*,6a*R*)-Octahydro-1-pentalenyl]-4-methylbenzenesulfonamide (1*R*,3a*R*,6a*R*)-32

TFA (314 μL, 4.08 mmol) was added dropwise to a stirred solution of Boc protected bicyclic sulfonamide **31** (129 mg, 0.34 mmol) in CH_2Cl_2 (1.5 mL) at 0°C under N_2. The resulting solution was allowed to warm to rt. After stirring for 2.5 h at rt, the solvent was evaporated under reduced pressure. Excess TFA was removed by azeotroping with $CHCl_3$ (4×5 mL) to give the crude product. Purification by flash chromatography on silica with petrol–Et_2O (1:1) as eluent gave bicyclic sulfonamide (1*R*,3a*R*,6a*R*)-**32** (72 mg, 76, 69% ee assumed) as a white solid, mp 100–101°C; R_F(1:1 petrol–Et_2O) 0.2; $[\alpha]_D=-11.0$ (*c* 1.0 in $CHCl_3$); IR (CH_2Cl_2) 3373, 2954, 1279, 1252, 1155 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) 7.79 (br d, 2H, *J*=8.0 Hz), 7.30 (br d, 2H, *J*=8.0 Hz), 5.19 (d, 1H, *J*=7.0 Hz), 3.13 (br quin., 1H, *J*=7.0 Hz), 2.49–2.35 (m, 1H), 2.43 (s, 3H), 2.19–2.08 (m, 1H), 1.90–1.77 (m, 1H), 1.74–1.64 (m, 1H), 1.62–1.15 (m, 7H), 1.12–0.97 (m, 1H); ^{13}C NMR (67.9 MHz, $CDCl_3$) 143.0, 138.0, 129.5, 127.0, 61.4, 50.6, 41.3, 33.7, 33.6, 31.5, 30.8, 25.5, 21.5; MS (CI, NH_3) 297 $(M+NH_4)^+$, 280 $(M+H)^+$; HRMS (CI, NH_3) *m/z* calcd for $C_{15}H_{21}NO_2S$ $(M+H)^+$ 280.1371, found 280.1366.

4.26. *N*-[2-Cyclopenten-1-yl]-4-methylbenzenesulfonamide *rac*-17

Using general procedure B, aziridine **7** (119 mg, 0.5 mmol), *sec*-butyllithium (1.16 mL of a 1.25 M solution in cyclohexane, 1.45 mmol) and TMEDA (222 μL, 1.45 mmol) in Et_2O (5 mL) gave the crude product. Purification by flash chromatography on silica with pentane–EtOAc (8:2) as eluent gave allylic sulfonamide *rac*-**17** (27 mg, 23%) as a colourless oil and $TsNH_2$ (33 mg, 38%) as a white solid.

4.27. *N*-[2-Cyclopenten-1-yl]-4-methylbenzenesulfonamide *rac*-17

Using general procedure C, aziridine **7** (119 mg, 0.5 mmol) and *sec*-butyllithium (1.16 mL of a 1.25 M solution in cyclohexane, 1.45 mmol) in Et_2O (5 mL) gave the crude product. Purification by flash chromatography on silica with pentane–EtOAc (8:2) as eluent gave allylic sulfonamide *rac*-**17** (9 mg, 8%) as a white solid and $TsNH_2$ (59 mg, 69%) as a white solid.

4.28. *N*-[2-Cyclopenten-1-yl]-4-methylbenzenesulfonamide *rac*-17

Using general procedure C, aziridine **7** (119 mg, 0.5 mmol) and *sec*-butyllithium (1.16 mL of a 1.25 M solution in cyclohexane, 1.45 mmol) in THF (5 mL) gave the crude product. Purification by flash chromatography on silica with pentane–EtOAc (8:2) as eluent gave allylic sulfonamide *rac*-**17** (12 mg, 10%) as a white solid and $TsNH_2$ (48 mg, 56%) as a white solid.

4.29. *N*-[2-Cyclohexen-1-yl]-4-methylbenzenesulfonamide *rac*-11

Using general procedure B, aziridine **8** (126 mg, 0.5 mmol), *sec*-butyllithium (1.19 mL of a 1.2 M solution in cyclohexane, 1.45 mmol) and TMEDA (222 μL, 1.45 mmol) in Et_2O (5 mL) gave the crude product. Purification by flash chromatography on silica with pentane–EtOAc (8:2) as eluent gave allylic sulfonamide *rac*-**11** (28 mg, 22%) as a pale yellow oil.

4.30. *N*-[2-Cyclohexen-1-yl]-4-methylbenzenesulfonamide *rac*-11

Using general procedure C, aziridine **8** (126 mg, 0.5 mmol) and *sec*-butyllithium (1.16 mL of a 1.25 M solution in cyclohexane, 1.45 mmol) in Et_2O (5 mL) gave the crude product. Purification by flash chromatography on silica with

pentane–EtOAc (8:2) as eluent gave allylic sulfonamide *rac*-**17** (72 mg, 57%) as a white solid and $TsNH_2$ (26 mg, 30%) as a white solid.

4.31. *N*-[2-Cyclohexen-1-yl]-4-methylbenzenesulfonamide *rac*-11

Using general procedure C, aziridine **8** (126 mg, 0.5 mmol) and *sec*-butyllithium (1.16 mL of a 1.25 M solution in cyclohexane, 1.45 mmol) in THF (5 mL) gave the crude product. Purification by flash chromatography on silica with pentane–EtOAc (8:2) as eluent gave allylic sulfonamide *rac*-**17** (5 mg, 4%) as a white solid and $TsNH_2$ (48 mg, 56%) as a white solid.

4.32. *N*-[(1*S**,2*R**,6*R**)-Bicyclo[4.1.0]hept-2-yl]-4-methylbenzenesulfonamide 36

Using general procedure C, aziridine **9** (133 mg, 0.5 mmol) and *sec*-butyllithium (1.16 mL of a 1.25 M solution in cyclohexane, 1.45 mmol) in Et_2O (5 mL) gave the crude product. Purification by flash chromatography on silica with petrol–Et_2O (1:1) as eluent gave aziridine **9** (23 mg, 17%) as a colourless oil; cyclo-propylsulfonamide **36** (30 mg, 23%) as a colourless oil, R_F(1:1 petrol–Et_2O) 0.22; IR (CH_2Cl_2) 3373, 2937, 2864, 1599, 1410, 1329, 1159 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.80 (br d, 2H, J=8.0 Hz), 7.30 (br d, 2H, J=8.0 Hz), 4.47 (d, 1H, J=8.0 Hz), 3.76–3.66 (m, 1H), 2.43 (s, 3H), 1.89–1.79 (m, 1H), 1.67–1.56 (m, 1H), 1.40–1.23 (m, 2H), 1.18–1.00 (m, 2H), 0.94–0.82 (m, 2H), 0.46 (dt, 1H, J=5.0, 9.0 Hz), 0.08 (q, 1H, J=5.0 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) 143.1, 138.6, 129.6, 127.0, 50.3, 28.4, 22.6, 21.6, 21.5, 15.9, 12.5, 8.0; MS (CI, NH_3) 283 $(M+NH_4)^+$, 266 $(M+H)^+$; HRMS (CI, NH_3) *m/z* calcd for $C_{14}H_{19}NO_2S$ $(M+H)^+$ 266.1215, found 266.1214; and $TsNH_2$ (27 mg, 31%) as a white solid.

4.33. *N*-[(1*R**,3a*S**,6a*S**)-Octahydro-1-pentalenyl]-4-methylbenzenesulfonamide *rac*-25

Using general procedure B, aziridine **10** (140 mg, 0.5 mmol), *sec*-butyllithium (1.2 mL of a 1.2 M solution in cyclohexane, 1.45 mmol) and TMEDA (219 μL, 1.45 mmol) in Et_2O (10 mL) gave the crude product. Purification by flash chromatography on silica with pentane–EtOAc (8:2) as eluent gave bicyclic sulfonamide *rac*-**25** (36 mg, 26%) as a pale yellow oil.

4.34. *N*-[(1*R**,3a*S**,6a*S**)-Octahydro-1-pentalenyl]-4-methylbenzenesulfonamide *rac*-25

Using general procedure C, aziridine **10** (140 mg, 0.5 mmol) and *sec*-butyllithium (1.16 mL of a 1.25 M solution in cyclohexane, 1.45 mmol) in Et_2O (5 mL) gave the crude product. Purification by flash chromatography on silica with pentane–EtOAc (8:2) as eluent gave aziridine **10** (32 mg, 23%) as a white solid and bicyclic sulfonamide *rac*-**25** (48 mg, 34%) as a white solid.

4.35. *N*-[(1*R**,3a*S**,6a*S**)-Octahydro-1-pentalenyl]-4-methylbenzenesulfonamide *rac*-25

Using general procedure C, aziridine **10** (140 mg, 0.5 mmol) and *sec*-butyl-lithium (1.16 mL of a 1.25 M solution in cyclohexane, 1.45 mmol) in THF (5 mL) gave the crude product. Purification by flash chromatography on silica with pentane–EtOAc (8:2) as eluent gave bicyclic sulfonamide *rac*-**25** (50 mg, 36%) as a white solid.

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