Ring-opening of *N*-tosylaziridines by heterosubstituted allyl anions. Application to the synthesis of azetidines and pyrrolidines

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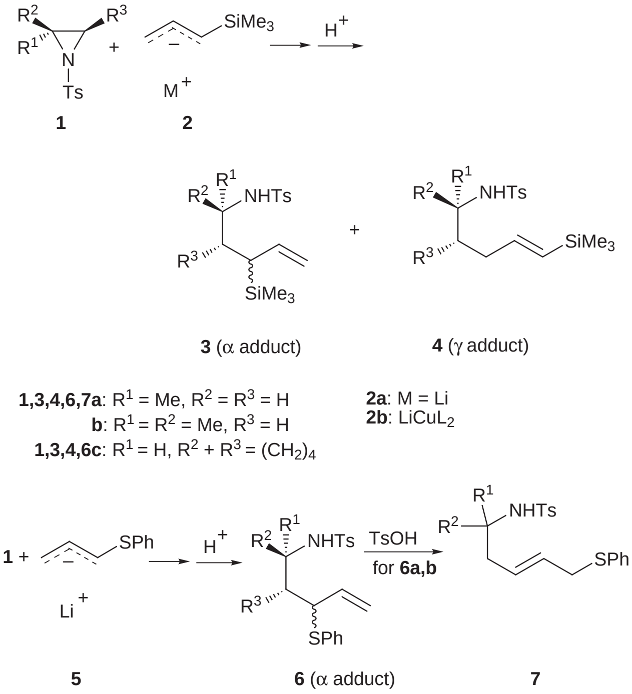
Ring opening of *N*-tosylaziridines by silyl- or phenylthio-substituted allyl anions gives *N*-(alk-4-enyl)tosylamides which may be cyclized to azetidines or pyrrolidines.

Recently, we reported ring-opening reactions of oxiranes by silyl[1]- and phenylthio-substituted allyl anions[2] which proved to offer convenient access to synthetically useful bishomoallyl alcohols. An obvious modification of the reaction would be to replace the epoxide by an aziridine which is activated by an electron-withdrawing nitrogen-substitutent with the tosyl residue likely to be the most promising candidate.[3] A first finding in this area was the unexpected reaction of 2-phenyl-1-tosylaziridine with the silyl-substituted allyl anion **2a** which serves as a base rather than as a nucleophile and induces annulation of the tosyl unit on the three-membered ring.[4] We now report on the reaction of hetero-substituted allyl anions with 2-alkyl-substituted *N*-tosylaziridines where the CH acidity should be reduced.

In fact, reaction of aziridines **1a**–**c** with allyl anions is controlled by the nucleophilic nature of the silyl-substituted species **2** (Scheme 1; Table 1) and likewise of the phenylthio-substituted allyl anion **5** (Scheme 1; Table 1) giving the desired ring-opened products. In both cases, the unsymmetrically substituted aziridines **1a,b** are attacked regioselectively at the less-substituted carbon C-3. The regioselectivity of the unsymmetrically substituted allyl components **2** is more complex. Thus, the reaction of allyl anion **2a** with 2-methyl-1-tosylaziridine **1a** gave after extensive chromatography only α adduct **3a**. However, the more sterically hindered aziridines **1b**,**c** produced increasing yields of γ adducts **4b**,**c**. For aziridine **1b** as starting material, use of the cuprate **2b** improved the γ selectivity and overall yields dramatically: addition of copper(I) iodide to a solution of **2** (M = Li) gave a ratio of **3b**:**4b** = 1:8 (yield 93%) and addition of copper(I) bromide–dimethyl sulfide led to a ratio of **3b**:**4b** = 1:6 (yield 89%).



Scheme 1 For details see Table 1.

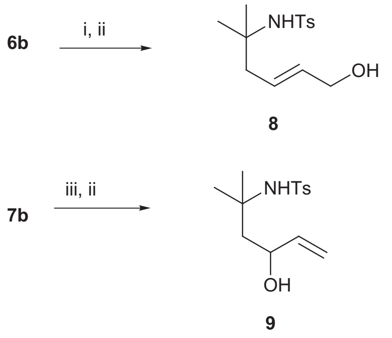
Table 1 Preparation of *N*-(alk-4-enyl)tosylamides

Aziridine	Carbanion	Product	Yield (%)	Product	Yield (%)
1a	**2a**	**3a**	17[a]	**4a**	—
1b	**2a**	**3b**	31	**4b**	24[b]
	2b		10–13		76–83[b]
1c	**2a**	**3c**	—	**4c**	34[b]
1a	**5**	**6a**	65[c]		
1b	**5**	**6b**	73		
1c	**5**	**6c**	99[d]		

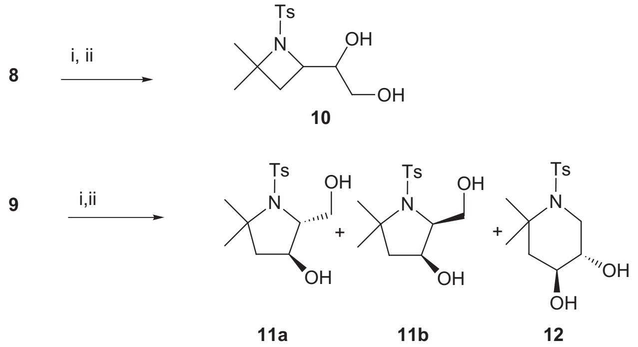
[a] Single diastereomer, isolated in pure form after extensive chromatography. [b] *E* isomer only. [c] Diastereomer ratio 1:1. [d] Diastereomer ratio 2:1.

The aziridines **1a**–**c** reacted smoothly with the sulfur-substituted allyl anion **5** to give in all examples the α adducts **6a**–**c** (Scheme 1; Table 1). Thus, for the sulfur case there is no effect of the aziridine substituents on the reaction pathway. Both allyl anions studied show higher α- or γ-selectivity with *N*-tosylaziridines than with the corresponding epoxides.[1,2] Moreover, we looked at some synthetic modifications of the ring-opened product **6b**. On treatment with toluene-*p*-sulfonic acid, **6a,b** did not cyclize, but rearranged with a 1,3 phenylthio shift to form the isomeric allyl sulfides **7**.[5] Interestingly, in contrast to the sulfur-substituted derivatives **6**, silyl-substituted tosylamides of type **3** have very recently been shown to undergo acid-induced cyclization to pyrrolidines.[6] Oxidation of **6b** and **7b** to the corresponding sulfoxides, followed by treatment with trimethyl phosphite gave the allyl alcohols **8** and **9**, respectively (Scheme 2).[7]

Epoxidation of allyl alcohol **8** and subsequent cyclization with sodium hydroxide gave the azetidine **10** (Scheme 3). Starting with allyl alcohol **9**, the same reaction sequence gave pyrrolidines **11a**,**b** and a small amount of piperidine **12**. The relative configurations of **11a**,**b** (yields 37%, 28%) were assigned based on a comparison of the chemical shifts,[8] while in the case



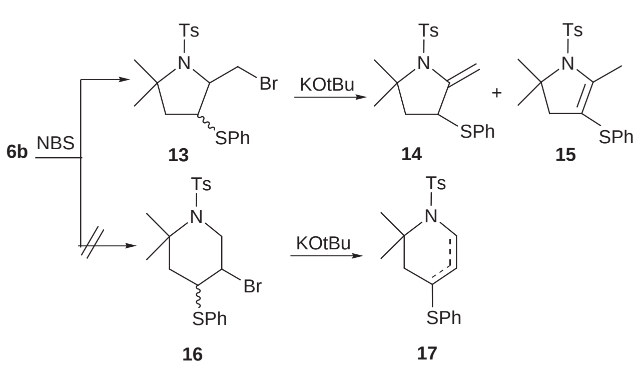
Scheme 2 *Reagents and conditions:* i, $NaIO_4$, $MeOH–H_2O$, 0→20 °C; ii, $P(OMe)_3$, MeOH, 60–70 °C, 6 h; iii, $NaIO_4$, $MeOH–H_2O$, room temperature→reflux (4 h).



Scheme 3 *Reagents and conditions:* i, MCPBA, $CHCl_3$, 0 °C→room temperature; ii, aqueous NaOH, 100 °C.

of **12** the coupling constant $^3J_{aa} = 8.6$ Hz indicates the *trans* configuration of the diol unit. Thus, starting from **9**, the intermediate epoxide does not only show the usual ring opening to the 5-*exo* products **11**, but also some competition by a 6-*endo* ring closure giving **12**, possibly due to steric interactions of the hydroxy and a methyl group in the transition state for one diastereomer.[9] So far, piperidines have only been obtained from (δ,ε-epoxyalkyl)tosylamides under reaction conditions which favoured S_N1-type ring opening.[10]

The reaction of **6b** with NBS led to the five-membered heterocycle **13** rather than the corresponding piperidine **16** (Scheme 4). In order to differentiate between the two possible ring sizes, hydrobromic acid was eliminated from **13** to form a mixture of **14** and **15** (combined yield 92%) both showing the expected set of signals in the ^1H NMR spectrum rather than the pattern characteristic for **17**. The thermodynamically favoured pyrroline **15** is obviously a secondary product of **14**. It is noteworthy that even under more forcing conditions, the isomeric allyl sulfide **7b** reacted neither with NBS nor with iodine.



Scheme 4

Experimental

General

^1H- and ^{13}C-NMR spectra were recorded with Bruker instruments AC 250 P or AMX 400 or a Varian spectrometer XL 200 using dilute solutions in $CDCl_3$, unless stated otherwise, with TMS as internal standard. Chemical shift values are given in ppm and coupling constants *J* in Hz. IR spectra were recorded using a Perkin-Elmer FT-IR instrument 1720 X or a Pye-Unicam spectrometer SP3-200. Elemental analyses were carried out at the Institut für Organische Chemie, Technische Universität Braunschweig. For column chromatography Merck silica gel 60 (70–230 mesh) was used.

The *N*-unsubstituted precursors of aziridines **1a**,[11] **1b**[12] and **1c**[13] were obtained as described in the literature and then tosylated using a standard protocol as reported for **1b**,**c**.[14] For **1a** also, data are available.[15]

Reaction of aziridines 1 with lithiated allyl(trimethyl)silane 2

To THF (15 cm^3), TMEDA (0.75 cm^3, 5 mmol) and protonated **2** (0.75 cm^3, 4.7 mmol) were added and the mixture cooled to −78 °C. Then a solution of *sec*-BuLi in hexane (5 mmol) was added dropwise. The reaction mixture was allowed to warm to −45 °C over 3 h. After cooling again to −78 °C, the aziridine (4 mmol) was added in one portion without solvent. The mixture was warmed to −30 °C over 2 h. Then it was cooled to −78 °C and poured into a mixture of saturated aqueous NH_4Cl solution (150 cm^3) and diethyl ether (150 cm^3). The organic phase was washed twice with saturated aqueous NaCl solution, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was filtered through a short column (eluent EtOAc–petroleum ether, 1:1). Solid crude products were finally recrystallized from petroleum ether. Separation of **3b** and **4b** was achieved by rotatory chromatography using a Chromatotron (eluent EtOAc–petroleum ether, 1:20); for yields see Table 1.

4-Methyl-*N*-(1-methyl-3-trimethylsilylpent-4-enyl)benzenesulfonamide 3a. Mp 109 °C (Found: C, 59.14; H, 8.82; N, 4.14; S 9.97; $C_{16}H_{27}NO_2SSi$ requires C, 59.03; H, 8.36; N, 4.30; S, 9.85%); ν_{max} (KBr)/cm^{-1} 3250, 2960, 1420, 1320, 1155, 1090, 835 and 665; δ_H (400 MHz) −0.10 (9 H, s, SiMe), 1.03 (3 H, d, *J* 6.6, NCMe), 1.40 (2 H, m, CH_2), 1.59 (1 H, ddd, *J* 11.0, 9.4 and 3.0, CHSi), 2.42 (3 H, s, Ts*Me*), 3.37 (1 H, m, CHN), 4.43 (1 H, d, *J* 8.7, NH), 4.60 (1 H, d, *J* 17.0, $=CH_2$), 4.79 (1 H, dd, *J* 10.7 and 1.5, $=CH_2$), 5.44 (1 H, ddd, *J* 17.0, 10.7 and 9.4, =CH), 7.28, 7.74 (each 2 H, d, *J* 8.1, aromatic CH); δ_C (100 MHz) −3.6 (SiMe), 21.5 (Ts*Me*), 22.4, 30.6, 49.3 (NC*Me*, CHN, CHSi), 36.2 (CH_2), 112.7 ($=CH_2$), 127.1, 129.5, 139.1 (=CH, aromatic CH), 138.3, 143.1 (aromatic C).

4-Methyl-*N*-(1,1-dimethyl-3-trimethylsilylpent-4-enyl)benzenesulfonamide 3b. Mp 55 °C (Found: C, 60.12; H, 8.58; N, 4.13; S 9.20; $C_{17}H_{29}NO_2SSi$ requires C, 60.13; H, 8.61; N, 4.12; S, 9.44%); ν_{max} (KBr)/cm^{-1} 3274, 2973, 2903, 1306, 1249, 1153 and 839; δ_H (250 MHz) −0.06 (9 H, s, SiMe), 1.13, 1.18 (each 3 H, s, NCMe), 1.54 (1 H, m, CH_2), 1.70 (2 H, m, CH_2, CHSi), 2.40 (3 H, s, Ts*Me*), 4.87 (2 H, m, $=CH_2$), 5.73 (1 H, m, =CH), 7.24, 7.74 (each 2 H, d, *J* 8.3, aromatic CH); δ_C (62.5 MHz) −3.5 (SiMe), 21.4 (Ts*Me*), 27.7, 28.3 (NC*Me*), 31.3 (CHSi), 42.0 (CH_2), 58.8 (CN), 112.3 ($=CH_2$), 127.0, 129.3 (aromatic CH), 141.0 (aromatic C), 141.5 (=CH), 142.6 (aromatic C).

4-Methyl-*N*-(1,1-dimethyl-5-trimethylsilylpent-4-enyl)-benzenesulfonamide 4b. Oil (Found: C, 60.56; H, 8.94; N, 3.98; S, 9.63; $C_{17}H_{29}NO_2SSi$ requires C, 60.13; H, 8.61; N, 4.12; S, 9.44%); ν_{max} (KBr)/cm^{-1} 3274, 2954, 1324, 1247, 1153 and 839; δ_H (250 MHz) 0.01 (9 H, s, SiMe), 1.15 (6 H, s, 2 × CH_3), 1.56 (2 H, m, CH_2CN), 2.05 (2 H, m, $CH_2C=$), 2.40 (3 H, s, Ts*Me*), 5.09 (1 H, s, NH), 5.54 (1 H, dt, *J* 18.5 and 1.4, =CHSi), 5.87

(1 H, dt, *J* 18.5 and 6.0, CH=CSi), 7.26, 7.78 (each 2 H, d, *J* 7.7, aromatic CH); δ_C (62.5 MHz) −1.3 (SiMe), 21.4 (Ts*Me*), 27.6 (2 × CH_3), 31.0, 41.5 (2 × CH_2), 56.8 (CN), 126.9, 129.4, 130.0 (=CH, aromatic CH), 140.7, 142.6 (aromatic C), 146.1 (=CH).

4-Methyl-*N*-[2-(3-trimethylsilylprop-2-enyl]cyclohexyl)-benzenesulfonamide 4c. Mp 116.5 °C (Found: C, 62.30; H, 8.70; N, 3.80; S, 8.74; $C_{19}H_{31}NO_2SSi$ requires C, 62.42; H, 8.55; N, 3.83; S, 8.77%); ν_{max} (KBr)/cm^{-1} 3230, 2880, 1420, 1310, 1140, 820 and 660; δ_H (400 MHz) 0.02 (9 H, s, SiMe), [0.83–0.97 (1 H, m), 1.03–1.14 (3 H, m), 1.17–1.27 (1 H, m), 1.57–1.59 (2 H, m), 1.70–1.79 (3 H, m), 2.43–2.48 (1 H, m), 2.81–2.89 (1 H, m), 5 × CH_2, 2 × CH], 2.42 (3 H, s, Ts*Me*), 4.54 (1 H, d, *J* 8.7, NH), 5.55 (1 H, d, *J* 18.3, =CHSi), 5.82 (1 H, ddd, *J* 18.3, 7.1 and 6.1, CH=CSi), 7.29, 7.76 (each 2 H, d, *J* 8.1, aromatic CH); δ_C (100 MHz) −1.2 (SiMe), 21.5 (Ts*Me*), 24.9, 25.1, 30.8, 34.3, 39.9 (5 × CH_2), 42.6, 57.2 (2 × CH), 126.9, 129.6, 132.2, 144.7 (=CH, aromatic CH), 138.5, 143.1 (aromatic C).

Reaction of aziridine 1b with cuprate 2b. Preferred formation of 4b

In an atmosphere of nitrogen, dry THF (15 cm^3) and TMEDA (0.5 cm^3, 3 mmol) were cooled to −78 °C. Then protonated **2** (0.5 cm^3, 3.1 mmol) and a solution of *sec*-BuLi in hexane (3.45 mmol) were added and the reaction mixture was allowed to warm to −40 °C over 4 h. Then CuBr·SMe_2 (322 mg, 1.57 mmol) was added at −78 °C and the mixture allowed to warm to −40 °C over 3 h. To the resulting grey solution of the cuprate aziridine **1b** (352 mg, 1.56 mmol) was added at −78 °C. After warming to rt overnight, the mixture was poured into saturated aqueous NH_4Cl–diethyl ether (40 cm^3 each). The solution was made alkaline with concentrated NH_3 and stirred for 3 h. Finally the organic phases were extracted twice with saturated aqueous NaCl solution, dried ($MgSO_4$) and the solvents evaporated. The residue was filtered through a short column (eluent EtOAc–petroleum ether, 1:1). The ^{1}H-NMR spectrum confirmed the residue (470 mg, 89%) to be a 1:6 mixture of **3b** and **4b**. Use of CuI instead of CuBr·SMe_2 gave **3b** and **4b** in 93% overall yield (ratio 1:8).

Reaction of aziridine 1 with lithiated allyl phenyl sulfide 5. Synthesis of 6a–c

In an atmosphere of nitrogen at −78 °C, THF (50 cm^3) was diluted with BuLi (22.5 cm^3 of a 1.6 M solution in hexane; 36 mmol). Then protonated **5** (5.4 g, 35.9 mmol) was added and the mixture allowed to warm to −30 °C over 1 h. Subsequently, an aziridine **1** (33.7 mmol) was added at −70 °C in one portion without solvent. After warming to −30 °C over 1.5 h, the aziridine dissolved. The mixture was cooled to −70 °C again and hydrolyzed by addition of saturated aqueous NH_4Cl solution. The mixture was washed with aqueous saturated NH_4Cl solution (100 cm^3) and diethyl ether (600 cm^3). The organic phase was extracted twice with saturated aqueous NaCl solution, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was filtered through a short column (eluent EtOAc–petroleum ether, 1:2) to give **6** as a colourless oil; for yields see Table 1.

4-Methyl-*N*-[1-methyl-3-(phenylthio)pent-4-enyl]benzene-sulfonamide 6a. Oil, 2 diastereomers, 1:1 (Found: C, 63.17; H, 6.42; N, 3.87; S, 17.66; $C_{19}H_{23}NO_2S_2$ requires C, 63.12; H, 6.41; N, 3.87; S, 17.74%); ν_{max} (film)/cm^{-1} 3250, 2960, 2910, 1320 and 1150; δ_H (200 MHz) 1.01–1.06 (3 H, m, NCMe), 1.60–1.74 (2 H, m, CH_2), 2.41, 2.43 (each 3 H, s, Ts*Me*), 3.42–3.70 (2 H, m, 2 × CH), [4.40 (1 H, d, *J* 8.9), 4.50 (1 H, d, *J* 10.0), NH], [4.75 (2 H, d, *J* 16.7), 4.94 (2 H, d, *J* 8.8), =CH_2], 5.45–5.67 (1 H, m, =CH), 7.24–7.36 (7 H, m, aromatic CH), [7.77 (2 H, d, *J* 8.3), 7.78 (2 H, d, *J* 8.3), aromatic CH]; δ_C (50 MHz) 21.5, 21.6, 22.1 (NC*Me*, Ts*Me*), 41.6, 41.9 (CH_2), 47.9, 48.1, 48.8 (CH), 115.7, 117.0 (=CH_2), 127.0, 127.1, 127.2, 127.4, 128.6, 128.7, 129.0, 129.7, 132.7, 133.3, 137.5, 138.0 (=CH, aromatic CH), 133.6, 133.8, 138.0, 138.1, 143.3, 143.5 (aromatic C).

4-Methyl-*N*-[1,1-dimethyl-3-(phenylthio)pent-4-enyl]-benzenesulfonamide 6b. Oil (Found: C, 64.15; H, 6.77; N, 3.52; S, 17.20; $C_{20}H_{25}NO_2S_2$ requires C, 63.96; H, 6.71; N, 3.73; S, 17.08%); ν_{max} (film)/cm^{-1} 3274, 2978, 1321 and 1152; δ_H (250 MHz) 1.23, 1.24 (each 3 H, s, NCMe), 1.90 (2 H, m, CH_2), 2.41 (3 H, s, Ts*Me*), 3.71 (1 H, m, CHS), 4.76 (1 H, d, *J* 17.0, =CH_2), 4.91 (1 H, dd, *J* 10.0 and 1.0, =CH_2), 5.72 (1 H, dt, *J* 17.0 and 9.6, =CH), 7.22–7.45 (7 H, m, aromatic CH), 7.75 (2 H, d, *J* 8.3, aromatic CH); δ_C (62.5 MHz) 21.4 (Ts*Me*), 27.8, 28.4 (NC*Me*), 46.7 (CH_2), 48.7 (CHS), 57.0 (CN), 115.6 (=CH_2), 126.9, 127.5, 128.7, 129.4, 133.4, 139.2 (=CH, aromatic CH), 133.8, 140.5, 142.8 (aromatic C).

4-Methyl-*N*-[2-(1-phenylthio)allylcyclohexyl]benzene-sulfonamide 6c. Oil, 2 diastereomers 2:1* (* indicates ^{1}H NMR signal of the minor diastereomer.) (Found: C, 65.95; H, 7.19; N, 3.41; S, 15.79; $C_{22}H_{27}NO_2S_2$ requires C, 65.80; H, 6.78; N, 3.49; S, 15.97%); ν_{max} (film)/cm^{-1} 3260, 2920, 2850, 1435, 1320, 1155, 1090 and 660; δ_H (400 MHz) 1.00–1.98 (9 H, m, 4 × CH_2, CH), 2.33* (3 H, s, Ts*Me*), 2.40 (3 H, s, Ts*Me*), 3.12 (1 H, m, CH), 3.50* (1 H, m, CH), 4.02* (1 H, dd, *J* 8.6 and 3.1, CHS), 4.21 (1 H, dd, *J* 8.6 and 2.5, CHS), 4.67–5.03 (3 H, m, NH, =CH_2), 5.69 (1 H, m, =CH), 7.14–7.34 (7 H, m, aromatic CH), 7.76–7.79 (2 H, m, aromatic CH); δ_C (100 MHz) 21.5 (Ts*Me*), 24.5, 24.7, 24.8, 24.8, 26.3, 26.7, 34.0, 34.3 (4 × CH_2), 47.2, 47.2, 51.5, 53.0, 54.1, 54.6 (3 × CH), 116.2, 118.6 (=CH_2), 126.5, 126.6, 126.9, 128.5, 128.7, 129.6, 129.7, 131.4, 131.9, 133.9, 137.0 (=CH, aromatic CH), 135.0, 135.1, 138.7, 143.1, 143.3 (aromatic C).

Rearrangement of 6a,b to 7

Equivalent amounts of **6** and TsOH·H_2O were dissolved in $CHCl_3$ (3 cm^3 mmol^{-1}) and the mixture stirred at rt for 4 d. Then the solvent was evaporated and the product purified by filtration through a short column (for **7a**, eluent EtOAc–petroleum ether, 1:10→1:15) or by stirring with MeOH, filtration, washing with MeOH and recrystallization from EtOAc–petroleum ether (for **7b**).

4-Methyl-*N*-[1-methyl-5-(phenylthio)pent-3-enyl]benzene-sulfonamide 7a. Yield 58%, oil (Found: C, 63.14; H, 6.51; N, 3.82; S, 17.84; $C_{19}H_{23}NO_2S_2$ requires C, 63.12; H, 6.41; N, 3.87; S, 17.74%); ν_{max} (film)/cm^{-1} 3260, 2960, 2920, 1320 and 1150; δ_H (200 MHz) 0.88 (3 H, d, *J* 6.6, MeCN), 2.00 (2 H, t, *J* 6.0, CH_2CN), 2.42 (3 H, s, Ts*Me*), 3.30 (1 H, m, CHN), 3.43 (2 H, d, *J* 6.7, CH_2S), 4.21 (1 H, d, *J* 8.0, NH), 5.16–5.49 (2 H, m, CH=CH), 7.24–7.33 (7 H, m, aromatic CH), 7.72 (2 H, d, *J* 8.5, aromatic CH); δ_C (50 MHz) 20.8 and 21.5 (*Me*CN, Ts*Me*), 36.2, 39.5 (2 × CH_2), 49.1 (CHN), 126.3, 127.0, 128.2, 128.9, 129.3, 129.6, 130.1 (CH=CH, aromatic CH), 135.6, 138.0, 143.2 (aromatic C).

***N*-[1,1-Dimethyl-5-(phenylthio)pent-3-enyl]-4-methylbenzene-sulfonamide 7b.** Yield 55%, mp 123–124 °C (Found: C, 63.87; H, 6.75; N, 3.86; S, 17.02; $C_{20}H_{25}NO_2S_2$ requires C, 63.96; H, 6.71; N, 3.73; S, 17.08%); ν_{max} (KBr)/cm^{-1} 3270, 2960, 1310 and 1140; δ_H (200 MHz) 1.00 (6 H, s, MeCN), 2.14 (2 H, d, *J* 6.6, CH_2CN), 2.42 (3 H, s, Ts*Me*), 3.52 (2 H, d, *J* 6.0, CH_2S), 4.29 (1 H, s, NH), 5.34–5.62 (2 H, m, CH=CH), 7.24–7.34 (7 H, m, aromatic CH), 7.74 (2 H, d, *J* 8.3, aromatic CH); δ_C (50 MHz) 21.5 (Ts*Me*), 27.3 (*Me*CN), 36.3, 45.6 (2 × CH_2), 56.4 (Me_2*C*N), 126.4, 127.0, 128.1, 128.9, 129.5, 130.1, 130.3 (CH=CH, aromatic CH), 135.5, 140.5, 142.8 (aromatic C).

Oxidative desulfurization of 6b, 7b *via* the sulfoxide to give alcohols 8, 9

To a suspension of **6b** or **7b** in MeOH (12 cm^3 mmol^{-1}) a solution of NaIO$_4$ (1.2 equivalents) in H$_2$O (4 cm^3 mmol^{-1}) was added dropwise (at 0 °C for **6b**). The reaction mixture was allowed to warm to rt overnight (for **6b**) or refluxed for 4 h (for **7b**), filtered and the residue washed twice with MeOH (2 cm^3 mmol^{-1} each). The combined solutions were concentrated, CHCl$_3$ was added to the residue and the mixture dried (MgSO$_4$ or Na$_2$SO$_4$). The dry solution was concentrated *in vacuo*.

The crude sulfoxide was dissolved in MeOH (7 cm^3 mmol^{-1}), trimethyl phosphite (8 equivalents) added, and the mixture stirred under N$_2$ at 60–70 °C for 6 h. After dilution with a little water, the solvent was evaporated and the residue purified by column chromatography (eluent EtOAc–petroleum ether, 1:2→1:1).

***N*-(5-Hydroxy-1,1-dimethylpent-3-enyl)-4-methylbenzenesulfonamide 8.** Yield 40%, mp 88.5–89 °C (Found: C, 59.96; H, 7.52; N, 4.75; S, 11.45; $C_{14}H_{21}NO_3S$ requires C, 59.34; H, 7.47; N, 4.94; S, 11.32%); ν_{max} (KBr)/cm^{-1} 3410, 3100, 2860, 1430, 1300 and 1130; δ_H (400 MHz) 1.16 (6 H, s, Me$_2$CN), 2.23 (2 H, d, *J* 6.1, CH$_2$CN), 2.42 (3 H, s, Ts*Me*), 4.09 (2 H, d, *J* 4.1, CH$_2$O), 5.69 (2 H, m, CH=CH), 7.28, 7.78 (each 2 H, d, *J* 8.3, aromatic CH); δ_C (100 MHz) 21.5 (Ts*Me*), 27.4 (*Me*CN), 45.8 (CH$_2$), 56.5 (Me$_2$*C*N), 63.2 (CH$_2$), 126.4, 127.0, 129.5, 134.1 (CH=CH, aromatic CH), 140.5, 142.9 (aromatic C).

***N*-(3-Hydroxy-1,1-dimethylpent-4-enyl)-4-methylbenzenesulfonamide 9.** Yield 62%, mp 82 °C (Found: C, 59.20; H, 7.63; N, 4.71; S, 11.45; $C_{14}H_{21}NO_3S$ requires C, 59.34; H, 7.47; N, 4.94; S, 11.32%); ν_{max} (KBr)/cm^{-1} 3430, 3250, 2960, 1400, 1310, 1130, 1090 and 650; δ_H (400 MHz) 1.25, 1.30 (each 3 H, s, MeCN), 1.44 (1 H, dd, *J* 14.8 and 2.0, CH$_2$), 1.76 (1 H, dd, *J* 14.8 and 10.7, CH$_2$), 2.41 (3 H, s, Ts*Me*), 4.45 (1 H, ddd, *J* 10.7, 6.0 and 2.0, CHO), 5.08 (1 H, d, *J* 10.2, =CH$_2$), 5.23 (1 H, d, *J* 17.3, =CH$_2$), 5.83 (1 H, ddd, *J* 17.3, 10.2 and 6.0, CH=), 7.27, 7.79 (each 2 H, d, *J* 8.1, aromatic CH); δ_C (100 MHz) 21.5 (Ts*Me*), 27.1, 28.7 (*Me*CN), 48.6 (CH$_2$), 56.3 (Me$_2$*C*N), 70.5 (CHO), 114.6 (=CH$_2$), 127.0, 129.5, 140.9 (CH=, aromatic CH), 142.6 (aromatic C).

Epoxidation and cyclization of 8, 9 to give heterocycles 10–12

N-(Hydroxyalkyl)sulfonamide **8** or **9** was dissolved in CHCl$_3$ (10 cm^3 mmol^{-1}) and a solution of MCPBA (1.1 equivalents) in CHCl$_3$ (3 cm^3 mmol^{-1}) added dropwise with stirring at 0 °C. The reaction mixture was allowed to warm to rt and after 1 d washed with aqueous NaHSO$_3$ solution, three times with saturated aqueous NaHCO$_3$ solution and finally once with saturated aqueous NaCl solution. After drying (MgSO$_4$) the solvent was evaporated and the crude epoxide stirred with a solution of NaOH (3.5 equivalents) in H$_2$O (1 cm^3 mmol^{-1}) at 100 °C for 5 min. After cooling to rt, the reaction mixture was extracted with CHCl$_3$ three times. The combined organic phases were washed with saturated aqueous NaCl solution and dried (MgSO$_4$). The solution was concentrated and the crude product purified by recrystallization from acetone–petroleum ether (for **10**) or by column chromatography (for **11, 12**; eluent CHCl$_3$–EtOAc, 2:1, then diethyl ether and finally EtOAc).

4-(1,2-Dihydroxyethyl-2,2-dimethyl-1-(4-methylphenylsulfonyl)azetidine 10. Yield 65% (based on **8**), mp 123 °C (Found: C, 56.00; H, 7.13; N, 4.60; S, 10.76; $C_{14}H_{21}NO_4S$ requires C, 56.17; H, 7.07; N, 4.68; S, 10.71%); ν_{max} (KBr)/cm^{-1} 3360, 2960, 1325 and 1150; δ_H (400 MHz) 1.33, 1.49 (each 3 H, s, MeCN), 1.76 (1 H, dd, *J* 10.7 and 8.6, CH$_2$CN), 2.02 (1 H, t, *J* 6.3, CH$_2$O*H*), 2.17 (1 H, dd, *J* 10.7 and 7.5, CH$_2$CN), 2.44 (3 H, s, Ts*Me*), 2.80 (1 H, d, *J* 4.6, CHO*H*), 3.64 (2 H, dd, *J* 6.3 and 5.5, C*H*$_2$OH), 3.95 (1 H, t, *J* 5.5, dd, *J* 4.6 and 2.5, CHO), 4.15 (1 H, ddd, *J* 8.6, 7.5 and 2.5, CHN), 7.33, 7.73 (each 2 H, d, *J* 8.1, aromatic CH); δ_C (100 MHz; acetone) 21.4 (Ts*Me*), 25.7, 30.0 (*Me*CN), 31.4 (*C*H$_2$CN), 61.3 (CH), 63.4 (CH$_2$OH), 68.6 (Me$_2$*C*N), 71.0 (CH), 128.6, 130.3 (aromatic CH), 138.7, 143.9 (aromatic C).

***trans*-2-Hydroxymethyl-5,5-dimethyl-1-(4-methylphenylsulfonyl)pyrrolidin-3-ol 11a.** Yield 15% (based on **9**), mp 134 °C (Found: C, 56.32; H, 7.28; N, 4.57; S, 10.68; $C_{14}H_{21}NO_4S$ requires C, 56.17; H, 7.07; N, 4.68; S, 10.71%); ν_{max} (KBr)/cm^{-1} 3480, 3340, 2970, 1320, 1150, 1125 and 665; δ_H (400 MHz) 1.50, 1.55 (each 3 H, s, MeCN), 1.81 (1 H, dd, *J* 13.4 and 3.6, C*H*$_2$CMe$_2$), 1.86 (1 H, d, *J* 3.6, CHO*H*), 2.12 (1 H, dd, *J* 13.4 and 5.3, C*H*$_2$CMe$_2$), 2.41 (3 H, s, Ts*Me*), 2.81 (1 H, t, *J* 5.8, CH$_2$O*H*), 3.65 (1 H, t, *J* 4.6, d, *J* 2.0, CHN), 3.74 (1 H, ddd, *J* 11.9, 5.8 and 4.6, C*H*$_2$OH), 3.81 (1 H, ddd, *J* 11.9, 5.8 and 4.6, C*H*$_2$OH), 4.28 (1 H, dddd, *J* 5.3, 3.6, 3.6 and 2.0, C*H*OH), 7.27, 7.79 (each 2 H, d, *J* 8.1, aromatic CH); δ_C (100 MHz) 21.9 (Ts*Me*), 28.3, 32.7 (*Me*CN), 49.2 (*C*H$_2$CMe$_2$), 64.3 (CH$_2$OH), 66.8 (*C*Me$_2$), 71.8 (CHN), 72.5 (CHOH), 127.8, 129.9 (aromatic CH), 138.8, 143.5 (aromatic C).

***cis*-2-Hydroxymethyl-5,5-dimethyl-1-(4-methylphenylsulfonyl)pyrrolidin-3-ol 11b.** Yield 28% (based on **9**), mp 158 °C (Found: C, 56.09; H, 7.25; N 4.39; S, 10.44; $C_{14}H_{21}NO_4S$ requires C, 56.17; H, 7.07; N, 4.68; S, 10.71%); ν_{max} (KBr)/cm^{-1} 3400, 3300, 2970, 1315, 1140, 1100 and 680; δ_H (400 MHz) 1.41, 1.65 (each 3 H, s, Me), 2.01 (2 H, d, *J* 7.6, C*H*$_2$CMe$_2$), 2.43 (3 H, s, Ts*Me*), 2.60 (1 H, dd, *J* 7.6 and 5.1, CH$_2$O*H*), 2.74 (1 H, d, *J* 6.1, CHO*H*), 3.70 (1 H, ddd, *J* 7.2, 5.1 and 3.5, CHN), 3.90 (1 H, ddd, *J* 11.9, 7.6 and 3.5, C*H*$_2$OH), 4.06 (1 H, ddd, *J* 11.9, 5.1 and 5.1, C*H*$_2$OH), 4.35 (1 H, t, *J* 7.6, dd, *J* 7.2 and 6.1, C*H*OH), 7.29, 7.75 (each 2 H, d, *J* 8.2, aromatic CH); δ_C (100 MHz; acetone) 21.8 (Ts*Me*), 28.4, 32.1 (*Me*CN), 49.3 (*C*H$_2$-CMe$_2$), 63.1 (CH$_2$OH), 64.9 (CHN), 70.3 (CHOH), 128.6, 130.7 (aromatic CH), 140.9, 144.2 (aromatic C).

***trans*-6,6-Dimethyl-1-(4-methylphenylsulfonyl)piperidine-3,4-diol 12.** Yield 4% (based on **9**), oil; δ_H (400 MHz) 1.14, 1.43 (each 3 H, s, Me), 1.58 (1 H, dd, *J* 13.2 and 11.2, C*H*$_2$CMe$_2$), 1.72 (1 H, dd, *J* 13.2 and 5.1, C*H*$_2$CMe$_2$), 2.42 (3 H, s, Ts*Me*), 2.97 (1 H, dd, *J* 13.0 and 10.4, CH$_2$N), 3.56 (1 H, ddd, *J* 10.4, 8.6 and 5.1, C*H*CH$_2$N), 3.68 (1 H, ddd, *J* 11.2, 8.6 and 5.1, C*H*CH$_2$CMe$_2$), 4.20 (1 H, dd, *J* 13.0 and 5.1, CH$_2$N), 7.28, 7.68 (each 2 H, d, *J* 8.6, aromatic CH); δ_C (100 MHz) 21.9 (Ts*Me*), 23.2, 30.3 (*Me*CN), 47.2, 47.6 (CH$_2$), 59.1 (*C*Me$_2$), 71.2, 73.6 (CH), 127.4, 130.1 (aromatic CH), 139.9, 143.7 (aromatic C).

5-Bromomethyl-2,2-dimethyl-1-(4-methylphenylsulfonyl)-4-(phenylthio)pyrrolidine 13

A solution of **6b** (140 mg, 0.373 mmol) in CHCl$_3$ (20 cm^3) was stirred with NBS (73 mg, 0.41 mmol) at rt for 5.5 h and then hydrolyzed with CHCl$_3$–saturated aqueous NaHCO$_3$ solution (60 cm^3, 1:1). The organic phase was extracted twice with a saturated aqueous NaCl solution, dried (Na$_2$SO$_4$) and concentrated *in vacuo*. The crude product (mixture of 2 diastereomers, 1:1) was purified by column chromatography (EtOAc–petroleum ether, 1:10→1:20) to give 53% of **13** as a single diastereomer (mp 99 °C) and a mixed fraction, ν_{max} (KBr)/cm^{-1} 2960, 1595, 1465, 1420, 1330, 1150, 1090, 1000, 745 and 670; δ_H (400 MHz) 1.60, 1.61 (each 3 H, s, Me), 1.97 (1 H, d, *J* 14.2, CH$_2$CS), 2.46 (1 H, dd, *J* 14.2 and 7.6, CH$_2$CS), 2.47 (3 H, s, Ts*Me*), 3.35 (1 H, t, *J* 10.9, CHN), 3.87–3.92 (3 H, m, CHS, CH$_2$Br), 7.14–7.16 (2 H, m, Ph), 7.24–7.27 (3 H, m, Ph), 7.29, 7.75 (each 2 H, d, *J* 8.1, aromatic CH); separate signals of the other diastereomer: 1.56, 1.57 (each 3 H, s, Me), 1.91 (1 H, m, CH$_2$CS), 2.10 (1 H, dd, *J* 11.2 and 7.6, CH$_2$CS), 2.41 (3 H, s, Ts*Me*), 3.24 (1 H, dd, *J* 10.7 and 10.7, CH$_2$Br), 3.54 (1 H, dd,

J 10.7 and 3.6, CH_2Br), 3.77 (1 H, d, J 10.7, 1 H, t, J 3.6, CHN), 4.77 (1 H, t, J 8.1, d, J 3.1, CHS), 7.80 (2 H, d, J 8.7, aromatic CH); δ_C (100 MHz) 21.6 (Ts*Me*), 28.3, 33.7 (*Me*CN), 34.2, 45.4 (2 × CH_2), 47.4 (CH), 66.8 (CN), 68.3 (CH), 127.6, 127.7, 128.9, 129.4, 131.9 (aromatic CH), 133.7, 138.2, 143.1 (aromatic C); other diastereomer: 21.6 (Ts*Me*), 25.6, 29.6 (*Me*CN), 32.2, 33.0 (2 × CH_2), 53.2, 57.9 (2 × CH), 68.4 (CN), 127.8, 128,1, 129.2, 129.5, 132.9 (aromatic CH), 132.8, 136.9, 143.4 (aromatic C); *m*/*z* (EI) 453.0431 (M^+. $C_{20}H_{24}BrNO_2S_2$ requires 453.0632).

Dehalogenation of 13 to give 14, 15

13 (234 mg, 0.51 mmol, mixture of diastereomers) was dissolved in *t*BuOH (5 cm^3). Then KO*t*Bu (200 mg, 1.78 mmol) was added and the mixture stirred under nitrogen at 60–70 °C for 2 h. After cooling to rt, the reaction mixture was hydrolyzed by pouring it into saturated aqueous NH_4Cl–diethyl ether solution (200 cm^3 each). The organic phase was washed once with saturated aqueous NaCl solution, dried (Na_2SO_4) and concentrated *in vacuo* to give a mixture of **14** and **15** (177 mg, 92%). Column chromatography (eluent EtOAc–petroleum ether, 1 : 10) gave 46 mg (24%) of pure **15** as a colourless oil, which was characterized spectroscopically.

2,2-Dimethyl-5-methylene-4-(phenylthio)-1-(4-methylphenylsulfonyl)pyrrolidine 14. δ_H (400 MHz) 1.50, 1.57 (each 3 H, s, MeCN), 2.11 (1 H, d, J 8.6, CH_2), 2.12 (1 H, d, J 7.6, CH_2), 2.42 (3 H, s, Ts*Me*), 4.61 (1 H, t, J 8.1, CHS), 4.85, 5.56 (each 1 H, s, =CH_2), 7.23–7.32 (7 H, m, aromatic CH), 7.68 (2 H, d, J 8.1, aromatic CH); δ_C (100 MHz) 21.5 (Ts*Me*), 25.8, 30.2 (2 × CH_3), 39.2 (CH_2), 61.3 (CHS), 68.2 (Me_2*C*N), 115.4 (=CH_2), 128.0, 128.1, 129.2, 129.22, 133. 2 (aromatic CH), 132.3, 137.3, 143. 2, 144.8 (R_2C=, aromatic C).

2,3-Dihydro-2,2,5-trimethyl-4-(phenylthio)-1-(4-methylphenylsulfonyl)pyrrole 15. δ_H (400 MHz) 1.62 (6 H, s, MeCN), 2.16 (3 H, t, J 2.0, =CMe), 2.43 (3 H, s, Ts*Me*), 2.48 (2 H, q, J 2.0, CH_2), 7.16–7.32 (7 H, m, aromatic CH), 7.73 (2 H, d, J 8.1, aromatic CH); δ_C (100 MHz) 14.3 (=C*Me*), 21.5 (Ts*Me*), 28.8 (NC*Me*), 49.4 (CH_2), 68.4 (Me_2*C*N), 125.8, 126.8, 127.5, 129.0, 129.7 (aromatic CH), 105.7, 135.7, 140.2, 143.3, 144.4 (R_2C=CR_2, aromatic C).

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