Pergamon

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Tetrahedron 59 (2003) 9729–9742

TETRAHEDRON

Organolithium-induced synthesis of acyclic unsaturated amino alcohols from epoxides of dihydropyrroles and tetrahydropyridines

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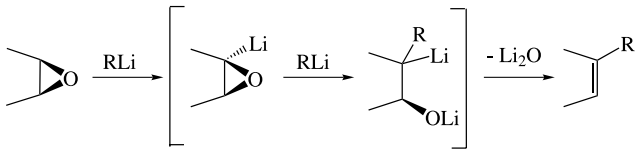
Received 2 July 2003; revised 3 September 2003; accepted 1 October 2003

Abstract—The alkylative double ring-opening of Bus-protected 2,5-dihydropyrrole epoxides **13** and **29** with organolithiums to give 3-substituted 1-aminobut-3-en-2-ols **13**–**19** and **30**–**32** are described. Bus-protected tetrahydropyridine epoxide **38** reacts with organolithiums to give 4-substituted 1-aminobut-4-en-3-ols **39** and tetrahydropyridinol **40**.

1. Introduction

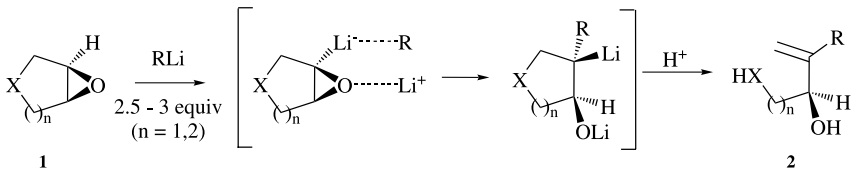
Epoxides are versatile synthetic intermediates.[1] Their reactions are dominated by cleavage of the strained three-membered ring by nucleophilic opening and acid or base-induced isomerization reactions. The alkylative deoxygenation of epoxides using organolithiums to give substituted alkenes (Scheme 1) was originally discovered by Crandall and Lin,[2] and a number of research groups have subsequently made contributions to this area.[3]



Scheme 1.

In one development of this methodology, we recently reported the alkylative deoxygenation of dihydrofuran and dihydropyran epoxides **1** to generate unsaturated diols **2** (Scheme 2, X=O).[4,5] This process most likely proceeds via α-deprotonation and insertion (possibly by a 1,2-metallate shift)[6] of a second equivalent of organolithium into the resulting lithiated epoxide, followed by elimination.

In connection with the above studies, we considered whether the chemistry outlined in Scheme 2 could be developed to provide unsaturated amino alcohols **2** (X=NR[1]).[7] The 1,2-amino alcohol motif is frequently found in bioactive natural products, many pharmaceutical agents and in useful synthetic intermediates, auxiliaries, and ligands in catalysis.[8] As a consequence, considerable importance is attached to new methods to access this moiety. However, it was unclear at the outset of the current work if the corresponding dihydropyrrole epoxide **3** would undergo initial deprotonation with an organolithium α-to the epoxide oxygen as desired, or α-to nitrogen to give **4** (Scheme 3),[9] the latter potentially giving pyrroles **6** via the allylic alkoxide **5**.[10]



Scheme 2.

Keywords: epoxides; organolithiums; amino alcohols; eliminations and alkenes.
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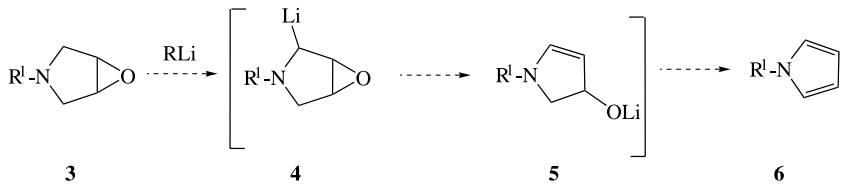
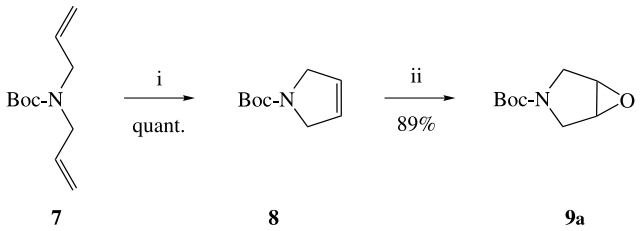
0040–4020/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2003.10.010



Scheme 3.

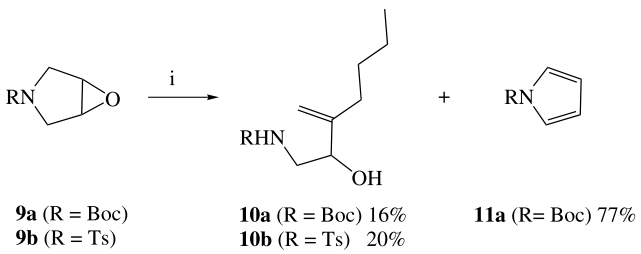
2. Results and discussion

Our initial investigations focused on the reductive alkylation of Boc-protected epoxide **9a** (Scheme 2).[11] Preparation of epoxide **9a** was readily achieved by ring-closing metathesis of commercially available *N*-Boc protected diallylamine **7**[12–14] and subsequent epoxidation (Scheme 4).[15]



Scheme 4. *Reagents and conditions*: (i) $(PCy_3)_2Cl_2Ru{=}CHPh$ (0.02 equiv.), CH_2Cl_2, 25°C, 14 h;[12] (ii) CF_3COCH_3 (11 equiv.), Na_2EDTA (0.002 equiv.), $NaHCO_3$ (8 equiv.), Oxone (5 equiv.), MeCN, 0°C, 14 h.[15]

Under conditions that led to clean formation of alkenediols from dihydrofuran epoxide **1** (Scheme 2, X=O, n=1),[4,5] addition of ^{n}BuLi (2.5 equiv.) to Boc-protected 2,5-dihydropyrrole epoxide **9a** gave mainly *N*-Boc pyrrole **11a** (77%), along with a small amount of the desired amino alcohol **10a** (16%, Scheme 5). Diagnostic proton NMR spectroscopic details for the amino alcohol **10a** are two one proton singlets (δ_H=5.13 and 4.92) for the vinylic protons and well defined signals for the protons attached to the oxygen and nitrogen bearing carbons [δ_H=4.18–4.10 (1H, m, CHO), 3.48–3.39 (1H, m, H of CH_2N) and 3.15–3.08 (1H, m, H of CH_2N)].



Scheme 5. *Reagents and conditions*: (i) ^{n}BuLi (3 equiv.), THF, −78°C, 1 h to 25°C, 1 h.

Further experimentation with Boc-protected epoxide **9a** is summarised in Table 1. Reversing the order of addition, that is dropwise addition of a solution of the epoxide **9a** to Bu^{n}Li at −78°C (THF, 1 h, followed by warming to 25°C), significantly reduced the formation of *N*-Boc pyrrole **11a** but the yield of amino alcohol **10a** was also very low (Table 1, entry 1). No *N*-Boc pyrrole **11a**, was isolated from similar reactions carried out in Et_2O, toluene or hexane (entries 2–4), with the best yield of amino alcohol **10a** (46%) being obtained in Et_2O (entry 2). In Et_2O the addition of a ligand (TMEDA, entry 5), variation of reaction temperature (entries 6 and 7), or extended reaction time (5 h at −78°C, entry 8) gave reduced yields of amino alcohol **10a**, whereas varying in the quantity of Bu^{n}Li (entries 9 and 10) made little difference to the yield of amino alcohol **10a**.

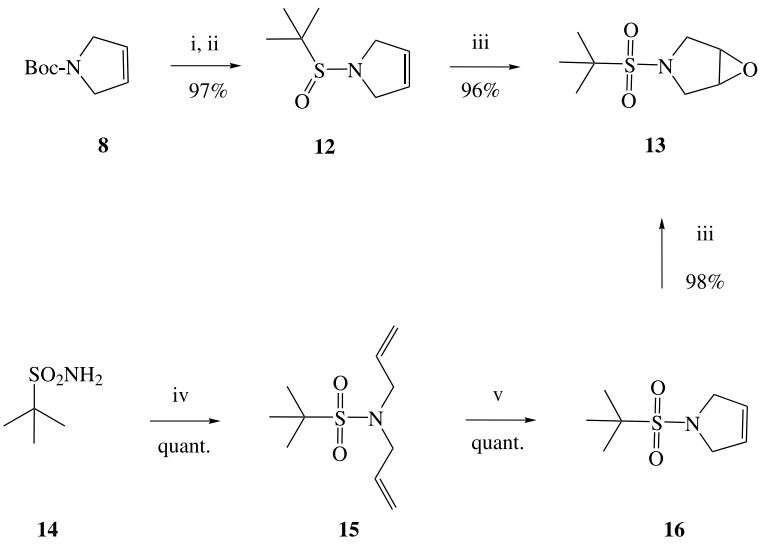
Variation of the organolithium under the conditions described in Table 1, entry 2 was examined. However, with Bu^{s}Li, Pr^{i}Li, Bu^{t}Li and Me_3SiCH_2Li, yields of the corresponding amino alcohols (16–22%) were significantly reduced compared to that found with Bu^{n}Li (46%); with Pr^{i}Li, Bu^{t}Li and Me_3SiCH_2Li, *N*-Boc pyrrole **11a** was also isolated in 22, 34 and 19% yields, respectively.

Table 1. Reaction of epoxide **9a** with Bu^{n}Li

Entry[a]	Bu^{n}Li (equiv)	Solvent	Temperature (°C)	Yield of **10a**[b] (%)	Yield of **11a**[b] (%)
1	3	THF	−78	9	22
2	3	Et_2O	−78	46	–
3	3	Toluene	−78	22	–
4	3	Hexane	−78	19	–
5[c]	3	Et_2O	−78	9	3
6	3	Et_2O	−50	22	–
7	3	Et_2O	−100	8[d]	22
8[e]	3	Et_2O	−78	26	–
9	2.2	Et_2O	−78	47	8
10	5	Et_2O	−78	48	15

[a] Reactions carried out by dropwise addition of a solution of the epoxide **9a** to ^{n}BuLi at −78°C (1 h, followed by warming to 25°C) unless stated otherwise.
[b] Isolated yields.
[c] TMEDA (3 equiv.) was also present.
[d] 45% Epoxide **9a** was recovered.
[e] After addition of Bu^{n}Li, reaction was maintained at −78°C for 5 h before warming.

We considered that an alternative protecting group might result in better yields of the desired amino alcohols. Organosulfonyl protection was examined with the view that pyrrole **6** by-product formation might be reduced, since deprotonation α-to N to give **4** (Scheme 3) could be relatively less favourable (compared to R^1=Boc), due to a potentially reduced sulfonamide co-ordinative effect with the organolithium. Using the conditions of Table 1, entry 2 with tosyl protected epoxide **9b** (Scheme 5) gave the corresponding amino alcohol **10b**, but in poor yield (20%, 36% based on recovered starting material). The use of 5 equiv. of Bu^{n}Li gave the amino alcohol **10b** in 31% yield with no recovery of starting epoxide, and in neither of these reactions was *N*-Ts pyrrole detected as a by-product. Although not probed experimentally, one possible reason for the recovery of starting tosyl-protected epoxide could be competing *ortho*-lithiation of the protecting group.[16] To avoid the latter issue we were attracted to the *tert*-butylsulfonyl (Bus) group, introduced by Weinreb and co-workers, as it is base stable and can be deprotected under



8 **12** **13** **14** **15** **16**

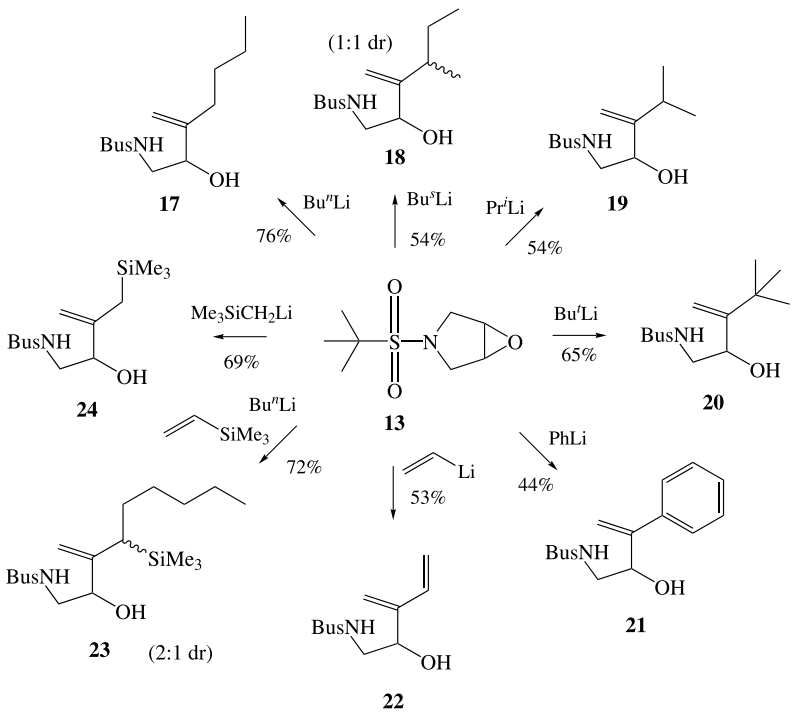
Scheme 6. *Reagents and conditions*: (i) TFA (19 equiv.), CH_2Cl_2, 25°C, 4 h; (ii) Et_3N (10 equiv.), CH_2Cl_2, 25°C, 1 h, then Bu^{t}SOCl[17] (2 equiv.), CH_2Cl_2, 0°C, 4 h; (iii) CF_3COCH_3 (11 equiv.), Na_2EDTA (0.002 equiv.), $NaHCO_3$ (8 equiv.), Oxone (5 equiv.), CH_3CN, 0°C, 14 h;[15] (iv) NaH (2.2 equiv.), DMF, 0°C, 1 h, then allyl bromide (2.2 equiv.), 0°C, 14 h; (v) $(PCy_3)_2Cl_2Ru{=}CHPh$ (0.02 equiv.), CH_2Cl_2, 25°C, 14 h.[12]

fairly mild acidic conditions.[17] The Bus-protected 2,5-dihydropyrrole epoxide **13** could be readily prepared in excellent yield, either from Boc-protected pyrroline **8** by a protecting group interchange, or from *tert*-butylsulfonamide **14**,[18] as indicated in Scheme 6.

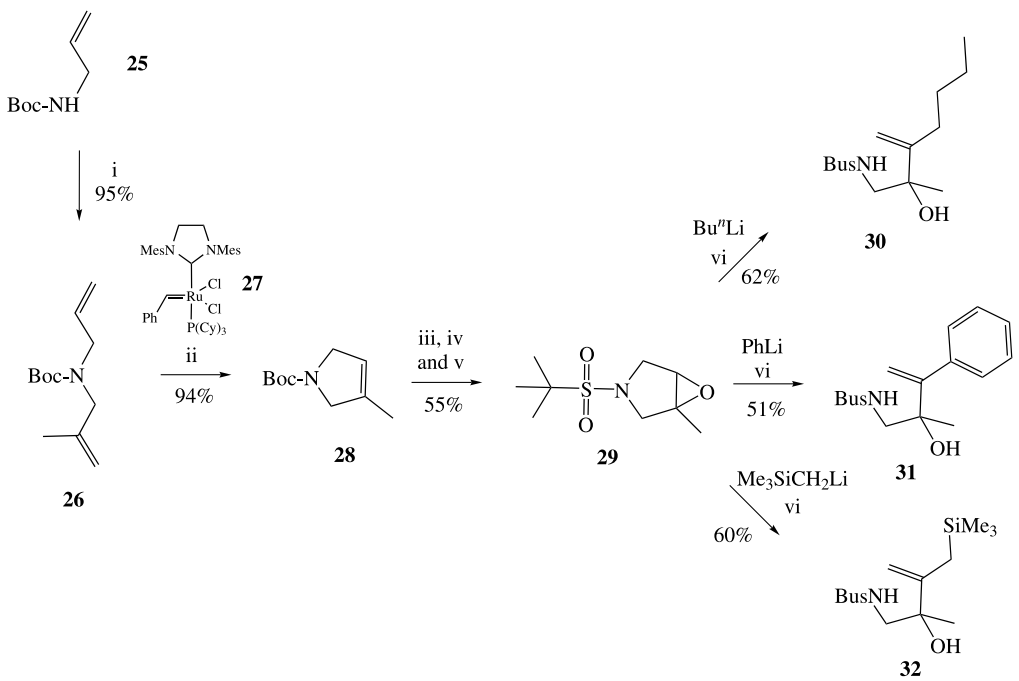
We were pleased to observe that reaction of *N*-Bus epoxide **13** with Bu^{n}Li under the best conditions found for *N*-Boc epoxide **9a** (Table 1, entry 2) gave a significant improvement in yield (76%) of the corresponding Bus-protected amino alcohol **17** (Scheme 7). The reaction of *N*-Bus epoxide **13** was then examined with other organolithiums (3 equiv.) to provide a range of 3-substituted 1-aminobut-3-en-2-ols **18**–**24** in generally satisfactory yields (Scheme 7).[7]

The synthesis of diene **22** is particularly noteworthy, since to the best of our knowledge this is the first report of reaction via α-lithiation of an epoxide with vinyllithium[3] and provides a new entry to conjugated dienes. Allylsilanes, of considerable utility in organic synthesis,[19] are also readily accessible, as indicated by the formation of **23** and **24**. Formation of allylsilane **23** makes use of the addition of organolithiums to vinylsilane to give substituted α-silyl anions[20] and in the present case allows a straightforward way to prepare more highly substituted allylsilanes.

In order to examine the scope of this chemistry with a trisubstituted epoxide, we investigated the methyl-substituted epoxide **29** (Scheme 8). The latter was synthesised via



Scheme 7.

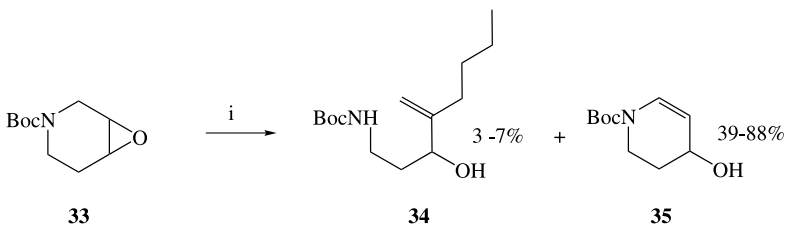


Scheme 8. *Reagents and conditions*: (i) NaH (2.2 equiv.), DMF, 0°C, 1 h, then 3-bromo-2-methylpropene (2.2 equiv.), 0°C, 14 h (ii) **27** (0.02 equiv.), CH_2Cl_2, 25°C, 14 h;[21,22] (iii) TFA (19 equiv.), CH_2Cl_2, 25°C, 4 h; (iv) Et_3N (10 equiv.), CH_2Cl_2, 25°C, 1 h, then Bu^{t}SOCl (2 equiv.), CH_2Cl_2, 0°C, 4 h; (v) CF_3COCH_3 (11 equiv.), Na_2EDTA (0.002 equiv.), $NaHCO_3$ (8 equiv.), Oxone (5 equiv.), CH_3CN, 0°C, 14 h;[15] (vi) RLi (3 equiv.), Et_2O, −78°C, 1 h.

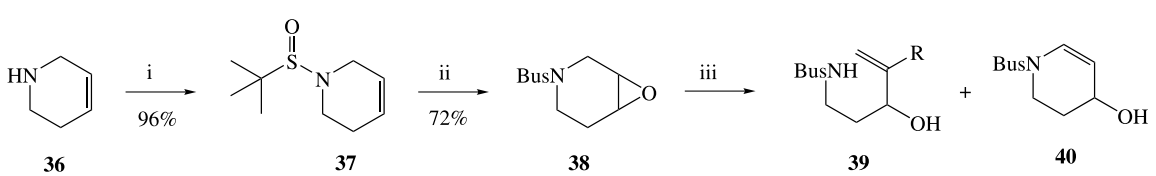
methallylation of commercially available Boc-protected allyl amine **25** and subsequent ring-closing metathesis. Protecting group interchange, oxidation and epoxidation gave epoxide **29** in 49% overall yield from Boc-protected allyl amine **25** (Scheme 8). The reductive alkylation conditions developed for the *N*-Boc epoxide **9** were applied to trisubstituted epoxide **29** and, pleasingly, gave in good yields the tertiary alcohols **30**–**32** with three representative organolithiums (Scheme 8).

Extension of the reductive alkylation process to produce 1,3-amino-alcohols from tetrahydropyridine epoxides was next examined (Scheme 2, X=NR[1], *n*=2). However, reaction of the known[23] Boc-protected epoxide **33** with ^{n}BuLi under the standard conditions [addition of the epoxide to the organolithium at −78°C (1 h) then warming to room temperature over 1 h] only resulted in 5% yield of the desired amino alcohol **34**, with the cyclic allylic alcohol **35** also being isolated in 39% yield (Scheme 9). Attempted variation of the reaction conditions [slow warm-up (16 h), warming to room temperature immediately after the addition of the epoxide, addition of MeOH after 1 h at −78°C, or addition of the organolithium to the epoxide at −78°C] failed to improve the yield of amino alcohol **34**, although the allylic alcohol **35** was isolated in up to 88% yield under the slow warm-up conditions.

Similarly to the earlier dihydropyrrole epoxide studies, the Bus-protected tetrahydropyridine epoxide **38**, readily prepared from 1,2,3,6-tetrahydropyridine **36** (Scheme 10), gave



Scheme 9. *Reagents and conditions*: (i) ^{n}BuLi (3 equiv.), Et_2O, −78°C, 1 h.



Scheme 10. *Reagents and conditions*: (i) Et_3N (10 equiv.), CH_2Cl_2, 25°C, 1 h, then Bu^{t}SOCl (2 equiv.), CH_2Cl_2, 0°C, 4 h; (ii) *m*CPBA (1.2 equiv.), CH_2Cl_2, 25°C, 1 h; (iii) RLi (3 equiv.), Et_2O, −78°C, 1 h.

a much improved yield (51%) of the desired amino alcohol **39** (R=Bu^n), although the corresponding cyclic allylic alcohol **40** was still observed (17%).

Interestingly, under otherwise identical conditions but using THF as the solvent, led to the cyclic alcohol **40** preferentially (65%, 3% of **39** R=Bu^n); use of toluene compared with Et_2O gave a higher isolated yield of the sought after amino alcohol **39** (65%, R=Bu^n), but a higher proportion of cyclic allylic alcohol **40** (25%). Use of LiCl as an additive in a reaction under otherwise standard conditions (Bu^{n}Li (3 equiv.), LiCl (3 equiv.), Et_2O at −78°C) gave only the desired amino alcohol **39** (R=Bu^n), with no cyclic allylic alcohol **40** observed; however, the yield of **39** (R=Bu^n) was reduced compared to the LiCl-free reaction (40% vs 51%).

A range of organolithiums were reacted with epoxide **38** in Et_2O (Table 2), and in most cases mixtures of amino alcohol **39** and cyclic allylic alcohol **40** were isolated, with the desired amino alcohol **39** usually being marginally preferred. Two notable exceptions were the use of MeLi (Table 2, entry 2) and PhLi (entry 6), where cyclic allylic alcohol **40** was exclusively or highly preferred, respectively.

Table 2. Reaction of epoxide **38** with a range of organolithiums

	RLi[a]	Yield of **39**[b] (%)	Yield of **40**[b] (%)
1	Bu^{n}Li	51	17
2	MeLi	–	100
3	Pr^{i}Li	23	–
4	Bu^{s}Li	41	34
5	Bu^{t}Li	45	41
6	PhLi	5	60
7	$TMSCH_2Li$	43	31

[a] Reactions carried out by dropwise addition of a solution of the epoxide **38** to RLi (3 equiv.) in Et_2O at −78°C (1 h, followed by warming to 25°C).
[b] Isolated yields.

The desired 1,3-amino alcohols, **34** and **39** respectively, arise from α-deprotonation of epoxide where the *N*-Boc and *N*-Bus groups direct the epoxide lithiation vicinal to themselves. A similar observation has been reported with the corresponding dihydropyran epoxides.[4] Competitive formation of the cyclic alcohols **35** and **40** possibly arises from deprotonation α-to the *N*-Boc and *N*-Bus groups, although an intermediate similar to **4** (Scheme 3) may be by-passed and the transformation may resemble more a (*syn*)[24] E2 elimination.[10b] The increased proportion of cyclic alcohols **35** and **40** in the reductive alkylation of tetrahydropyridine epoxides **33** and **38**, compared with pyrrole by-product formation from dihydropyrrole epoxides, may reflect the reduced acidity of the α-hydrogens of an epoxide fused to a six-membered rather than a five-membered ring.[10b]

3. Conclusion

In conclusion, we have demonstrated that treatment of dihydropyrrole and tetrahydropyridine epoxides with a diverse array of organolithiums provides a new route to substituted unsaturated amino alcohols. Extension of this process to other epoxides and organolithiums, asymmetric transformations[4,5] and manipulations of these adducts towards targets of biological interest are currently under investigation.

4. Experimental

4.1. General

All reactions requiring anhydrous conditions were conducted in flame- or oven- dried apparatus under an atmosphere of argon. Syringes and needles for the transfer of reagents were dried at 140°C and allowed to cool in a desiccator over P_2O_5 before use. Ethers were distilled from sodium benzophenone ketyl under argon; CH_2Cl_2, pentane, hexane and toluene from CaH_2 under argon. External reaction temperatures are reported unless stated otherwise. Reactions were monitored by TLC using commercially available aluminium-backed plates, pre-coated with a 0.25 mm layer of silica containing fluorescent indicator (Merck). Column chromatography was carried out on Kieselgel 60 (40–63 μm). Petrol refers to the fraction with bp 40–60°C. Melting points were determined using a Gallenkamp hot stage apparatus and are uncorrected. Elemental analyses were performed by Elemental Microanalysis Limited, Okehampton, Devon, UK. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ using Bruker JEOL EX400 or Bruker AM500 spectrometers. Chemical shifts are reported relative to $CDCl_3$ [δ_H 7.26, δ_C (central line of triplet) 77.0]. Coupling constants (*J*) are given in Hz, to the nearest 0.5 Hz. Mass spectra were obtained by the EPSRC National Mass Spectrometry Service Centre at the University of Swansea, using a Micromass Quattro II low resolution triple quadrupole mass spectrometer or, for accurate masses, using a Finnigan MAT 900 XLT high resolution double focusing mass spectrometer with tandem Ion Trap.

4.1.1. *tert*-Butyl 6-oxa-3-aza-bicyclo[3.1.0]hexane-3-carboxylate 9a.[11,14] 1,1,1-Trifluoroacetone (5.93 mL, 65.0 mmol) was added dropwise to a stirred solution of alkene **8** (1.00 g, 5.91 mmol) and aq. Na_2EDTA (4.00×10^{-4} mol dm^{-3}, 29.5 mL, 0.0118 mmol) in MeCN (50 mL) at 0°C. A mixture of $NaHCO_3$ (3.85 g, 47.3 mmol) and Oxone® (18.2 g, 29.5 mmol) was then added portionwise over a period of 1 h. After 1.5 h, the reaction mixture was diluted with water (50 mL), filtered and extracted with CH_2Cl_2 (3×50 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give a yellow oil. Purification of the residue by column chromatography [elution gradient 30–60% Et_2O in petrol] gave epoxide **9a** (1:1 mixture of rotamers) as a clear colourless oil (0.97 g, 89%); R_f 0.20 (50% Et_2O in petrol); ν_{max} (film)/cm^{-1} 3051, 2976, 2876, 1698, 1423, 1389, 1338, 1174, 1116, 1027 and 964; δ_H (500 MHz) 3.78 (1H, d, *J*=13.0 Hz, H of CH_2N), 3.66 (1H, d, *J*=13.0 Hz, H of CH_2N), 3.63 (2H, d, *J*=3.5 Hz, CHO), 3.27 (2H, dd, *J*=13.0, 3.5 Hz, H of CH_2N) and 1.40 (9H, s, $C(CH_3)_3$); δ_C (125 MHz) 154.6 (C=O), 79.6 ($C(CH_3)_3$), 55.4 (CHO), 54.9 (CHO), 47.1 (CH_2N), 46.7 (CH_2N) and 28.3 ($C(CH_3)_3$); *m/z* [EI +] 185 (100%, MH$^+$) and 170 (50) (Found: MH$^+$, 185.1055. $C_9H_{16}NO_3$ requires 185.1052).

4.1.2. Typical experimental procedure for reductive alkylations: *tert*-butyl (2-hydroxy-3-methyleneheptyl) carbamate 10a. A solution of *N*-Boc epoxide **9a** (0.20 g, 1.09 mmol) in Et_2O (8 mL) was added dropwise to a stirred solution of Bu^{n}Li (2.30 mol dm^{-3} in petrol, 1.42 mL, 3.26 mmol) in Et_2O (1 mL) at −78°C. After 1 h at −78°C the reaction was warmed to 25°C over 1 h and then sat. aq. NH_4Cl (5 mL) was added. The reaction mixture was extracted with Et_2O (3×10 mL) and the combined organic extracts were washed with sat. aq. $NaHCO_3$ (15 mL), brine (15 mL), dried ($MgSO_4$) and evaporated under reduced pressure. Purification of the residue by column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **10a** as a white solid (0.122 g, 46%); R_f 0.20 (40% Et_2O in petrol); mp 78.0–80.0°C; ν_{max} (film)/cm^{-1} 3408, 3085, 2960, 2931, 2873, 1694, 1055, 1514, 1468, 1436, 1392, 1367, 1340, 1273, 1252, 1172, 1110, 1073 and 980; δ_H (500 MHz) 5.13 (1H, s, H of CH_2=), 4.94–4.86 (1H, br s, NH), 4.92 (1H, s, H of CH_2=), 4.18–4.10 (1H, m, CHO), 3.48–3.39 (1H, m H of CH_2N), 3.15–3.08 (1H, m, H of CH_2N), 2.45 (1H, br, s, OH), 2.18 (1H, dt, J=15.5, 7.5 Hz, H of CH_2C=), 1.98 (1H, dt, J=15.5, 7.5 Hz, H of CH_2C=), 1.46–1.42 (11H, m, $C(CH_3)_3$, $CH_2CH_2CH_3$), 1.39–1.33 (2H, m, CH_2CH_3) and 0.92 (3H, t, J=7.5 Hz, $(CH_2)_2CH_3$); δ_C (125 MHz) 162.1 (C=O), 150.0 (C=), 110.0 (CH_2=), 79.5 ($C(CH_3)_3$), 74.2 (CHO), 45.3 (CH_2N), 31.9 (CH_2C=), 30.0 ($CH_2CH_2CH_3$), 28.2 ($C(CH_3)_3$), 22.4 (CH_2CH_3) and 13.8 ($(CH_2)_2CH_3$); *m/z* [EI +] 244 (30%, MH$^+$) and 188 (15); *m/z* [EI −] 318 (60%), 242 (98, M−H) and 89 (100) (Found: MH$^+$, 244.1915. $C_{13}H_{26}NO_3$ requires 244.1912).

4.1.3. *tert*-Butyl (2-hydroxy-4-methyl-3-methylenehexyl)carbamate 2 (X=*N*Boc, *n*=1, R=^{s}Bu). Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Boc epoxide **9a** (0.05 g, 0.27 mmol) in Et_2O (3 mL) was treated with ^{s}BuLi (1.40 mol dm^{-3} in light petroleum, 0.58 mL, 0.82 mmol). Column chromatography [elution gradient 30–60% Et_2O in light petroleum] gave amino alcohol **2** (X=*N*Boc, *n*=1, R=^{s}Bu) (1:1 mixture of diastereomers A:B) as a white solid (0.01 g, 16%); R_f 0.21 (40% Et_2O in petrol); mp 83.0–85.0°C; ν_{max} (KBr)/cm^{-1} 3413, 2966, 2931, 2876, 2361, 1694, 1512, 1456, 1392, 1367, 1251, 1172, 1081 and 903; δ_H (400 MHz) 5.18 (1H, s, H of CH_2=), 4.97–4.93 (2H, m, H of CH_2=, NH), 4.21–4.10 (1H, m, CHO), 3.52–3.37 (1H, m, CH_2N of A), 3.12–2.92 (1H, m, CH_2N of B), 2.40 (1H, br, s, OH), 2.04–1.95 (1H, m, CHC=), 1.47–1.42 (11H, m, $C(CH_3)_3$, CH_2CH_3), 1.07 (1.5H, d, J=7.0 Hz, $CHCH_3$ of A), 1.02 (1.5H, d, J=7.0 Hz, $CHCH_3$ of B), 0.90 (1.5H, t, J=6.0 Hz, CH_2CH_3 of A) and 0.85 (1.5H, t, J=6.0 Hz, CH_2CH_3 of B); δ_C (100 MHz) 161.2 (C=O), 155.1 (C=), 108.1 (CH_2=), 79.5 ($C(CH_3)_3$), 73.8 (CHO of A), 73.4 (CHO of B), 45.9 (CH_2N of A), 45.7 (CH_2N of B), 38.0 (CHC= of A), 37.5 (CHC= of B), 29.7 (CH_2CH_3 of A), 28.5 (CH_2CH_3 of B), 28.3 ($C(CH_3)_3$), 21.0 ($CHCH_3$ of A), 19.6 ($CHCH_3$ of B), 12.0 (CH_2CH_3 of A) and 11.6 (CH_2CH_3 of B); *m/z* [CI+(NH_3)] 244.2 (48%, MH$^+$) 205 (80), 189 (68), 172 (21), 144 (20), and 128 (100) (Found: MH$^+$, 244.1910. $C_{13}H_{25}NO_3$ requires 244.1912).

4.1.4. *tert*-Butyl (2-hydroxy-4-methyl-3-methylene-pentyl)carbamate 2 (X=*N*Boc, *n*=1, R=^{i}Pr). Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Boc epoxide **9a** (0.20 g, 1.09 mmol) in Et_2O (8 mL) was reacted with ^{i}PrLi (1.50 mol dm^{-3} in hexane, 2.17 mL, 3.26 mmol). Column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **2** (X=*N*Boc, *n*=1, R=^{i}Pr) as a white solid (0.055 g, 22%); R_f 0.23 (40% Et_2O in petrol); mp 76.0–76.5°C; ν_{max} (KBr)/cm^{-1} 3407, 3092, 2966, 2874, 1694, 1515, 1456, 1393, 1367, 1252, 1172, 1098, and 1075; δ_H (400 MHz) 5.12 (1H, s, H of CH_2=), 5.03 (1H, br s, NH), 4.97 (1H, s, H of CH_2=), 4.17 (1H, br, d, J=19.0 Hz, CHO), 3.44–3.38 (1H, m, CH_2N), 3.07–3.01 (1H, m, CH_2N), 2.66 (1H, br s, OH), 2.24 (1H, septet, J=7.0 Hz, CHC=), 1.43 (9H, s, $C(CH_3)_3$), 1.51 (3H, d, J=7.0 Hz, $CHCH_3$) and 1.32 (3H, d, J=7.0 Hz, $CHCH_3$); δ_C (100 MHz) 156.6 (C=O), 156.3 (C=), 107.9 (CH_2=), 79.5 ($C(CH_3)_3$), 73.3 (CHO), 45.9 (CH_2N), 30.7 (CHC=), 28.3 ($C(CH_3)_3$), 23.0 (CH_3CH) and 22.0 (CH_3CH); *m/z* [CI+(NH_3)] 230 (10%, MH$^+$), 191 (17), 175 (22), 131 (17), 166 (38), 114 (100), 112 (36) and 52 (74) (Found: MH$^+$, 230.1758. $C_{12}H_{24}NO_3$ requires 230.1756).

4.1.5. *tert*-Butyl (2-hydroxy-4-methyl-3-methylene-pentyl)carbamate 2 (X=*N*Boc, *n*=1, R=^{t}Bu). Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Boc epoxide **9a** (0.05 g, 0.27 mmol) in Et_2O (3 mL) was reacted with ^{t}BuLi (1.70 mol dm^{-3}in hexane, 0.477 mL, 0.82 mmol). Column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **2** (X=*N*Boc, *n*=1, R=^{t}Bu) as a white solid (0.013 g, 19%); R_f 0.22 (40% Et_2O in petrol); mp 86.0–87.0°C; ν_{max} (KBr)/cm^{-1} 3405, 3096, 2969, 2873, 1695, 1639, 1510, 1457, 1392, 1366, 1251, 1173, 1071 and 955; δ_H (400 MHz) 5.18 (1H, s, H of CH_2=), 5.12 (1H, s, H of CH_2=), 5.00 (1H, br, s, NH), 4.38–4.32 (1H, m, CHO), 3.39–3.34 (1H, m, H of CH_2N), 3.07–3.03 (1H, m, H of CH_2N), 2.09 (1H, br, s, OH), 1.46 (9H, s, $OC(CH_3)_3$) and 1.12 (9H, s, $C(CH_3)_3$); δ_C (100 MHz) 160.0 (C=O), 153.3 (C=), 108.8 (CH_2=), 79.8 ($OC(CH_3)_3$), 69.6 (CHO), 47.73 (CH_2N), 35.4 ($C(CH_3)_3$), 28.9 ($C(CH_3)_3$) and 28.3 ($OC(CH_3)_3$); *m/z* [EI +] 244 (50%, MH$^+$) 228 (17), 205 (82), 189 (71), 172 (22), 149 (18) and 128 (100) (*m/z* [CI+(NH_3)] Found: MH$^+$, 244.1913. $C_{13}H_{26}NO_3$ requires 244.1912).

4.1.6. *tert*-Butyl (2-hydroxy-4-methyl-3-methylene-pentyl)carbamate 2 (X=*N*Boc, *n*=1, R=CH_2TMS). Following the general procedure for (2-hydroxy-3-methyl-ene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Boc epoxide **9a** (0.10 g, 0.54 mmol) in Et_2O (8 mL) was reacted with $TMSCH_2Li$ (1.0 mol dm^{-3} in pentane, 1.63 mL, 1.63 mmol). Column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **2** (X=*N*Boc, *n*=1, R=CH_2TMS) as a white solid (0.025 g, 17%); R_f 0.22 (40% Et_2O in petrol); mp 73.5–74.5°C; (Found: C, 57.1; H, 9.9; N, 5.1. $C_8H_{13}NO_2Si$ requires C, 57.1; H, 10.0; N, 5.1%); ν_{max} (KBr)/cm^{-1} 3385, 2978, 2933, 1695, 1514, 1455, 1393, 1367, 1251, 1171 and 1010; δ_H (400 MHz) 5.00 (1H, s, H of CH_2=), 4.99 (1H, br s, NH), 4.75 (1H, s, H of CH_2=), 4.03–4.01 (1H, m, CHO), 3.48–3.43 (1H, m, H of CH_2N), 3.12–3.02 (1H, m, H of CH_2N), 2.58 (1H, br, s, OH), 1.74 (1H, d, J=14.0 Hz, H of CH_2TMS), 1.44 (9H, s, $C(CH_3)_3$), 1.38 (1H, d, J=14.0 Hz, H of CH_2TMS) and 0.04

(9H, s, TMS); δ_C (100 MHz) 156.7 (C=O), 147.1 (C=), 108.0 (CH_2=), 79.6 ($C(CH_3)_3$), 74.9 (CHO), 45.3 (CH_2N), 28.3 ($C(CH_3)_3$), 23.0 (CH_2TMS) and −1.4 (TMS); *m/z* [EI −] 272 (100%, M−H) and 126 (12) (*m/z* [CI+(NH_3)] Found: MH^+, 274.1836. $C_{13}H_{28}NO_3Si$ requires 274.1838).

4.1.7. 3-(Toluene-4-sulfonyl)-6-oxa-3-azabicyclo[3.1.0]-hexane 9b. A solution of 1-[(4-methylphenyl)sulfonyl]-2,5-dihydro-1*H*-pyrrole[25] (0.92 g, 4.13 mmol) and aq. Na_2EDTA (4×10^{-4} mol dm^{-3}, 20.6 mL, 0.008 mmol) in acetonitrile (70 mL) was cooled to 0°C. 1,1,1-Trifluoroacetone (4.06 mL, 45.4 mmol) was added dropwise to this homogeneous solution. A mixture of $NaHCO_3$ (2.77 g, 33.0 mmol) and Oxone® (12.7 g, 20.6 mmol) was then added portionwise over a period of 1 h. After 4 h, a mixture of $NaHCO_3$ (2.77 g, 33.0 mmol) and Oxone® (12.7 g, 20.6 mmol) was added and the reaction was then stirred overnight. The reaction mixture was then diluted with water (50 mL), filtered and extracted with CH_2Cl_2 (3×50 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give the title epoxide as a white crystalline solid (0.97 g, 98%), which did not require further purification; R_f 0.18 (50% Et_2O in petrol); mp 124.0–124.5°C; (Found: C, 55.4; H, 5.4; N, 5.7. $C_{11}H_{13}NO_3S$ requires C, 55.2; H, 5.5; N, 5.9%); ν_{max} (KBr)/cm^{-1} 3063, 2932, 2876, 1747, 1597, 1495, 1457, 1406, 1332, 1257, 1228, 1159, 1101, 1010 and 892; δ_H (400 MHz) 7.24 (2H, d, *J*=8.0 Hz, 2×H of Ar), 7.44 (2H, d, *J*=8.0 Hz, 2×H of Ar), 3.70 (2H, d, *J*=12.0 Hz, 2×H of CH_2N), 3.67 (2H, s, 2×CHO), 3.35 (2H, d, *J*=12.0 Hz, 2×H of CH_2N) and 2.41 (3H, s, CH_3); δ_C (100 MHz) 143.6 (SO_2C), 134.5 (CH_3C), 129.6 (CH of Ar), 127.2 (CH of Ar), 55.1 (CHO), 48.7 (CH_2N) and 21.5 (CH_3); *m/z* [CI+(NH_3)] 257 (100%, MNH_4^+), 240 (14, MH^+) and 86 (10) (Found: MH^+, 240.0692. $C_{11}H_{14}NO_3S$ requires 240.0694).

4.1.8. *N*-(2-Hydroxy-3-methylene-heptyl)-4-methylbenzenesulfonamide 10b. Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-tosyl epoxide **9b** (0.10 g, 0.42 mmol) in Et_2O (8 mL) was reacted with ^{n}BuLi (2.46 mol dm^{-3} in hexane, 0.510 mL, 1.26 mmol). Column chromatography [elution gradient 30–70% Et_2O in petrol] gave amino alcohol **10b** as a white solid (0.039 g, 31%); R_f 0.18 (50% Et_2O in petrol); mp 92.5–93.0°C; ν_{max} (KBr)/cm^{-1} 3488, 3293, 2957, 2927, 2872, 2858, 1663, 1636, 1498, 1458, 1396, 1366, 1309, 1548, 1127, 1090, 1042 and 891; δ_H (400 MHz) 7.85 (2H, d, *J*=8.0 Hz, 2×H of Ar), 7.33 (2H, d, *J*=8.0 Hz, 2×H of Ar), 5.05 (1H, s, H of CH_2=), 5.03–4.98 (1H, m, NH), 4.93 (1H, s, H of CH_2=), 4.26–4.10 (1H, m, CHO), 3.21–3.13 (1H, m, H of CH_2N), 2.90–2.82 (1H, m, H of CH_2N), 2.41 (3H, s, CH_3 of Ar), 2.22 (1H, br, s, OH), 1.97 (1H, dt, *J*=15.5, 7.5 Hz, H of CH_2C=), 1.84 (1H, dt, *J*=15.5, 7.5 Hz, H of CH_2C=), 1.41–1.34 (4H, m, $CH_2CH_2CH_3$, CH_2CH_3) and 0.89 (3H, t, *J*=7.0 Hz, $CH_3(CH_2)_3$); δ_C (100 MHz) 148.7 (SO_2C), 143.5 (C=), 136.7 (CH_3C), 129.7 (CH of Ar), 127.1 (CH of Ar), 110.8 (CH_2=), 72.9 (CHO), 47.5 (CH_2N), 31.8 (CH_2C=), 30.9 ($CH_2CH_2CH_3$), 22.4 (CH_2CH_3), 21.5 (CH_3 of Ar) and 13.9 ($CH_3(CH_2)_3$); *m/z* [CI+(NH_3)] 315 (80%, MNH_4^+), 300 (23), 298 (41, MH^+), 280 (21), 190 (30), 189 (100), 146 (16), 144 (70), 142 (22), 128 (60), 126 (23) and 111 (36) (Found: MNH_4^+, 315.1738. $C_{15}H_{27}N_2O_3S$ requires 315.1742).

4.1.9. 1-(2-Methyl-propane-2-sulfinyl)-2,5-dihydro-1*H*-pyrrole 12. Alkene **8**[11,14] (1.00 g, 5.91 mmol) in CH_2Cl_2 (100 mL) was stirred with TFA (8.65 mL, 112 mmol) at room temperature for 4 h. The solvent was removed under reduced pressure. The residue was then co-evaporated with toluene (15 mL) to give the desired amine as a black oil (0.40 g, quant.). No other purification was required; ν_{max} (film)/cm^{-1} 3422, 1678, 1435, 1205 and 1144; δ_H (500 MHz) 8.73 (2H, br s, NH_2), 5.92 (2H, s, 2× CH=) and 4.16 (4H, s, 2×CH_2N); δ_C (125 MHz) 124.7 (CH=) and 52.6 (CH_2N); *m/z* [EI +] 68 (100%, MH^+), 51 (48), 45 (76) and 41 (72) (Found: MH^+, 68.0501. C_4H_8N requires 68.0500).

To a solution of the above amine (0.40 g, 5.91 mmol) in CH_2Cl_2 (45 mL) at 25°C was added dropwise Et_3N (8.24 mL, 59.1 mmol). After 1 h the reaction was cooled to 0°C and ice-cold *tert*-butylsulfinyl chloride[17] (1.66 g, 11.8 mmol) in CH_2Cl_2 (5 mL) was added. After 1 h (TLC monitoring, 30% Et_2O in petrol), the mixture was diluted with sat. aq. $NaHCO_3$ (30 mL). The aqueous layer was then extracted with CH_2Cl_2 (3×10 mL). The organic extracts were combined, dried ($MgSO_4$) and concentrated under reduced pressure to give a brown oil. Purification of the residue by column chromatography [SiO_2, elution gradient 0–30% Et_2O in petrol] gave the sulfinamide **12** as a clear colourless oil (0.99 g, 97%); R_f 0.30 (30% Et_2O in petrol); ν_{max} ($CHCl_3$)/cm^{-1} 3460, 2959, 2915, 2857, 1716, 1644, 1474, 1390, 1363, 1345, 1301, 1175, 1107, 1070 and 1028; δ_H (400 MHz) 5.71 (2H, s, 2×CH=), 4.26–4.23 (2H, s, 2×H of CH_2N), 3.87–3.83 (2H, s, 2×H of CH_2N) and 1.14 (9H, s, $C(CH_3)_3$); δ_C (100 MHz) 126.5 (CH=) 57.4 ($C(CH_3)_3$), 54.7 (CH_2N) and 23.1 ($C(CH_3)_3$); *m/z* [CI+(NH_3)] 191 (28%, MH_4^+), 174 (89, MH^+), 158 (13), 72 (25), 70 (100), 68 (94) and 52 (26) (Found: MH^+, 174.0959. $C_8H_{16}NOS$ requires 174.0953).

4.1.10. 2-Methyl-propane-2-sulfonic acid diallylamide 15. ^{t}BuSO$_2$NH$_2$ **14**[18] (0.695 g, 5.07 mmol) was added dropwise to a solution of NaH (0.45 g, 60% dispersion in mineral oil, 11.2 mmol) in DMF (70 mL) at 25°C. After 1 h the reaction was cooled to 0°C and allyl bromide (0.97 mL, 11.2 mmol) was added. After 1 h the reaction was quenched with MeOH (10 mL) and the residue was diluted with H_2O (70 mL) and washed with Et_2O (4×50 mL). The organic phases were combined, dried (Na_2SO_4) and evaporated under reduced pressure to give a yellow oil. Purification of the residue by column chromatography [elution gradient 0–40% Et_2O in petroleum] gave the diene **15** as a clear colourless oil (1.10 g, quant.); R_f 0.8 (40% Et_2O in petrol); ν_{max} (film)/cm^{-1} 3082, 2984, 2927, 2872, 1642, 1482, 1453, 1438, 1420, 1395, 1364, 1335, 1317, 1217, 1204, 1162, 1125, 1045 and 995; δ_H (400 MHz) 5.93–5.69 (2H, m, CH=), 5.24–5.12 (4H, m, CH_2=), 3.82 (4H, d, *J*=6.0 Hz, CH_2) and 1.38 (9H, s, $C(CH_3)_3$); δ_C (100 MHz) 133.4 (CH_2=), 119.1 (CH=), 61.1 ($C(CH_3)_3$), 49.8 (CH_2) and 24.5 ($C(CH_3)_3$); *m/z* [CI+(NH_3)] 235 (63%, MNH_4^+), 218 (47, MH^+), 98 (98.2), 82 (11), 58 (22) and 52 (12) (Found: MH^+, 218.1214. $C_{10}H_{20}NO_3S$ requires 218.1215).

4.1.11. 1-(2-Methyl-propane-2-sulfonyl)-2,5-dihydro-1*H*-pyrrole 16. Diene **15** (0.16 g, 0.74 mmol) was added to a homogeneous purple-black solution of

$(PCy_3)_2Cl_2Ru{=}CHPh$[12] (0.01 g, 0.01 mmol) in anhydrous CH_2Cl_2 (20 mL) under argon. The resulting mixture was stirred at 25°C for 14 h, after which time TLC showed complete consumption of starting material (eluent 50% Et_2O in petrol). The reaction was quenched by exposure to air for ~2 h and then evaporated under reduced pressure. Purification of the residue by column chromatography [elution gradient 0–30% Et_2O in petrol] gave alkene **16** as a clear colourless oil (0.14 g, 100%); R_f 0.54 (40% Et_2O in petrol); δ_H (400 MHz) 5.77 (2H, s, CH=), 4.30 (4H, s, CH_2N) and 1.42 (9H, s, $C(CH_3)_3$); δ_C (100 MHz) 125.5 (CH=), 60.6 ($C(CH_3)_3$), 56.6 (CH_2N) and 24.3 ($C(CH_3)_3$); *m/z* [CI+(NH_3)] 207 (26%, MNH_4^+), 190 (26, MH^+), 70 (63) and 68 (38) (Found: MH^+, 190.0899. $C_8H_{16}NO_2S$ requires 190.0902).

4.1.12. 3-(2-Methyl-propane-2-sulfonyl)-6-oxa-3-aza-bicyclo[3.1.0]hexane 13. *Method 1*. 1,1,1-Trifluoroacetone (10.8 mL, 121 mmol) was added dropwise to a stirred solution of sulfinamide **12** (1.90 g, 11.0 mmol) and aq. Na_2EDTA (4×10^{-4} mol dm^{-3}, 54.9 mL, 0.02 mmol) in MeCN (150 mL) at 0°C. A mixture of $NaHCO_3$ (6.54 g, 87.9 mmol) and Oxone® (33.8 g, 54.9 mmol) was then added portionwise over a period of 1 h. After 4 h, a mixture of $NaHCO_3$ (6.54 g, 87.9 mmol) and Oxone® (33.8 g, 54.9 mmol) was added and the reaction was stirred overnight. The reaction mixture was diluted with water (50 mL), filtered and extracted with CH_2Cl_2 (3×50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to give a yellow solid. Purification of the residue by column chromatography [elution gradient 0–60% Et_2O in petrol] gave epoxide **13** as a white solid (2.16 g, 96%); R_f 0.11 (50% Et_2O in petrol); mp 106.0–106.5°C; (Found: C, 46.5; H, 7.6; N, 6.8. $C_8H_{15}NO_3S$ requires C, 46.8; H, 7.4; N, 6.8%); ν_{max} (film)/cm^{-1} 3063, 2984, 2939, 2878.5, 1910, 1731, 1642, 1482, 1464, 1407, 1366, 1309, 1254, 1228, 1195, 1135, 1090, 1011 and 962; δ_H (500 MHz) 3.92 (2H, br, d, *J*=12.0 Hz, 2×H of CH_2N), 3.70 (2H, s, 2×CHO), 3.44 (2H, d, *J*=12.0 Hz, 2×H of CH_2N) and 1.39 (9H, s, $C(CH_3)_3$); δ_C (100 MHz) 79.0 ($C(CH_3)_3$), 55.5 (CHO), 49.9 (CH_2N) and 24.4 ($C(CH_3)_3$); *m/z* [CI+(NH_3)] 223 (100%, MNH_4^+), 170 (30), 86 (37), 70 (23), 68 (28) and 52 (32) (Found: MNH_4^+, 223.1111. $C_8H_{19}N_2O_3S$ requires 223.1116).

Method 2. 1,1,1-Trifluoroacetone (0.521 mL, 5.82 mmol) was added dropwise to a stirred solution of alkene **16** (0.10 g, 0.53 mmol) and aq. Na_2EDTA (4×10^{-4} mol dm^{-3}, 2.65 mL, 0.001 mmol) in MeCN (8 mL) at 0°C. A mixture of $NaHCO_3$ (0.356 g, 4.23 mmol) and Oxone® (1.63 g, 2.65 mmol) was then added portionwise over a period of 1 h. After 4 h, a mixture of $NaHCO_3$ (0.356 g, 4.23 mmol) and Oxone® (1.63 g, 2.65 mmol) was added and the reaction was stirred overnight. The reaction mixture was diluted with water (5 mL), filtered and extracted with CH_2Cl_2 (3×5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to give a yellow solid. Purification of the residue by column chromatography [elution gradient 0–60% Et_2O in petrol] gave epoxide **13** as a white solid (0.11 g, 98%); data as above.

4.1.13. 2-Methyl-propane-2-sulfonic acid (2-hydroxy-3-methyleneheptyl)amide 17. Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **13** (0.10 g, 0.49 mmol) in Et_2O (8 mL) was reacted with Bu^nLi (2.50 mol dm^{-3} in pentane, 0.585 mL, 1.46 mmol). Column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **17** as a white solid (0.098 g, 76%); R_f 0.13 (40% Et_2O in petrol); mp 87.0–87.5°C; (Found: C, 54.3; H, 9.5; N, 5.2. $C_{12}H_{25}NO_3S$ requires C, 54.7; H, 9.6; N, 5.3%); ν_{max} (KBr)/cm^{-1} 3488, 3297, 2958, 2932, 2873, 1480, 1458, 1405, 1366, 1307, 1209, 1126 and 1029; δ_H (400 MHz) 5.15 (1H, s, H of CH_2=), 4.98 (1H, s, H of CH_2=), 4.53–4.51 (1H, m, NH), 4.25–4.22 (1H, m, CHO), 3.43–3.36 (1H, m, H of CH_2N), 3.14–3.08 (1H, m, H of CH_2N), 2.31 (1H, br, s, OH), 2.09 (1H, dt, *J*=16.0, 8.0 Hz, H of CH_2C=), 2.00 (1H, dt, *J*=16.0, 8.0 Hz, H of CH_2C=), 1.48–1.31 (13H, m, $C(CH_3)_3$, $CH_2CH_2CH_3$, CH_2CH_3) and 0.94 (3H, t, *J*=7.5 Hz, $CH_3(CH_2)_2$); δ_C (100 MHz) 150.0 (C=), 110.0 (CH_2=), 79.5 ($C(CH_3)_3$), 74.2 (CHO), 45.3 (CH_2N), 31.9 (CH_2C=), 30.0 ($CH_2CH_2CH_3$), 28.2 ($C(CH_3)_3$), 22.4 (CH_2CH_3), and 13.8 ($(CH_2)_2CH_3$); *m/z* [CI+(NH_3)] 281 (53%, MNH_4^+), 264 (20, MH^+), 246 (13), 169 (100), 155 (33), 146 (40), 128 (94), 114 (29), 100 (25), 86 (19) and 72 (40) (Found: MNH_4^+, 281.1892. $C_{12}H_{29}N_2O_3S$ requires 281.1899).

4.1.14. 2-Methyl-propane-2-sulfonic acid (2-hydroxy-4-methyl-3-methylenehexyl)amide 18. Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **13** (0.10 g, 0.49 mmol) in Et_2O (8 mL) was reacted with Bu^sLi (1.40 mol dm^{-3} in light petroleum, 1.05 mL, 1.46 mmol). Column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **18** (1:1 mixture of diastereomers A/B) as a white solid (0.069 g, 54%); R_f 0.21 (50% Et_2O in petrol); mp 87.5–89.0°C; ν_{max} (KBr)/cm^{-1} 3433, 3248, 2974, 2935, 2877, 1648, 1480, 1431, 1396, 1366, 1301, 1233, 1119, 1074 and 1035; δ_H (400 MHz) 5.18 (1H, d, *J*=8.5 Hz, H of CH_2=), 4.96–4.93 (2H, m, H of CH_2=, NH), 4.21–4.16 (1H, m, CHO), 3.38–2.64 (1H, m, CH_2N of A), 3.05–3.00 (1H, m, CH_2N of B), 2.87 (1H, br s, OH), 1.99 (0.5H, sextet, *J*=7.0 Hz, $CHCH_3$ of A), 1.97 (0.5H, sextet, *J*=7.0 Hz, $CHCH_3$ of B), 1.57–1.29 (11H, m, CH_2CH_3, $C(CH_3)_3$), 1.05 (3H, d, *J*=7.0 Hz, $CHCH_3$ of A), 1.01 (3H, d, *J*=7.0 Hz, $CHCH_3$ of B), 0.87 (1.5H, t, *J*=4.0 Hz, CH_2CH_3 of A) and 0.82 (1.5H, t, *J*=4.0 Hz, CH_2CH_3 of B); δ_C (100 MHz) 154.6 (C= of A), 154.5 (C= of B), 109.4 (CH_2= of A), 109.3 (CH_2= of B), 74.0 (CHO of A), 73.5 (CHO of B), 59.9 ($C(CH_3)_3$), 49.9 (CH_2N of A), 49.7 (CH_2N of B), 38.3 ($CHCH_3$ of A), 37.7 ($CHCH_3$ of B), 29.5 (CH_2CH_3 of A), 28.5 (CH_2CH_3 of B), 24.2 ($C(CH_3)_3$), 20.9 ($CHCH_3$ of A), 19.6 ($CHCH_3$ of B), 12.0 (CH_2CH_3 of A) and 11.6 (CH_2CH_3 of B); *m/z* [CI+(NH_3)] 281 (26%, MNH_4^+), 264 (42, MH^+), 169 (15), 155 (49), 144 (19), 128 (68) and 111 (100) (Found: MNH_4^+, 281.1900. $C_{12}H_{29}N_2O_3S$ requires 281.1899).

4.1.15. 2-Methyl-propane-2-sulfonic acid (2-hydroxy-4-methyl-3-methylenepentyl)amide 19. Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **13** (0.10 g, 0.49 mmol) in Et_2O (8 mL) was reacted with Pr^iLi (1.70 mol dm^{-3}in light petroleum, 0.861 mL, 1.46 mmol). Column chromatography [elution gradient 30–60% Et_2O in

petrol] gave amino alcohol **19** as a white solid (0.066 g, 54%); R_f 0.21 (50% Et_2O in petrol); mp 88.5–90.0°C; (Found: C, 52.6; H, 9.2; N, 5.7. $C_{11}H_{23}NO_3S$ requires C, 53.0; H, 9.3; N, 5.6%); ν_{max} (KBr)/cm^{-1} 3494, 3295, 3093, 2963, 2934, 2875, 1717, 1646, 1480, 1463, 1434, 1397, 1366, 1307, 1210, 1126, 1095, 1072, 1023 and 964; δ_H (400 MHz) 5.15 (1H, s, H of CH_2=), 5.01 (1H, s, H of CH_2=), 4.91–4.84 (1H, m, NH), 4.27–4.25 (1H, m, CHO), 3.45–3.33 (1H, m, H of CH_2N), 3.09–3.01 (1H, m, H of CH_2N), 2.23 (1H, septet, J=7.0 Hz, C*H*$(CH_3)_2$), 1.39 (9H, s, $C(CH_3)_3$), 1.19 (3H, d, J=7.0 Hz, CHC*H*$_3$) and 1.17 (3H, d, J=7.0 Hz, CHC*H*$_3$); δ_C (100 MHz) 156.1 (C=), 109.1 (CH_2=), 73.9 (CHO), 60.4 (*C*$(CH_3)_3$), 50.3 (CH_2N), 31.4 (*C*H$(CH_3)_2$), 24.6 (C(*C*$H_3)_3$), 23.3 (CH*C*H_3) and 22.4 (CH*C*H_3); *m/z* [CI+(NH_3)] 267 (36%, MNH_4^+), 250 (51, MH^+), 223 (21), 169 (22), 155 (61), 130 (33), 114 (98), 97 (100), 86 (18) and 70 (13) (Found: MNH_4^+, 267.1734. $C_{11}H_{27}N_2O_3S$ requires 267.1742).

4.1.16. 2-Methyl-propane-2-sulfonic acid (2-hydroxy-4,4-dimethyl-3-methylene-pentyl)-amide 20. Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **13** (0.10 g, 0.49 mmol) in Et_2O (8 mL) was reacted with Bu^{t}Li (2.5 mol dm^{-3} in light petroleum, 0.585 mL, 1.46 mmol). Column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **20** as a white solid (0.083 g, 65%); R_f 0.15 (40% Et_2O in petrol); mp 92.5–93.0°C; ν_{max} (KBr)/cm^{-1} 3498, 3301, 3092, 2954, 2932, 2881, 1720, 1642, 1483, 1461, 1440, 1395, 1367, 1301, 1207, 1129, 1096, 1072, 1024 and 967; δ_H (400 MHz) 5.19–5.11 (2H, m, H of CH_2=, NH), 5.09 (1H, s, H of CH_2=), 4.41–4.33 (1H, m, CHO), 3.34–3.25 (1H, m, H of CH_2N), 3.11–3.03 (1H, m, H of CH_2N), 2.90–2.75 (1H, m, OH), 1.36 (9H, s, $SO_2C(CH_3)_3$) and 1.09 (9H, s, $C(CH_3)_3$); δ_C (100 MHz) 158.9 (C=), 109.2 (CH_2=), 70.4 (CHO), 59.9 (SO_2C $(CH_3)_3$), 51.8 (CH_2N), 35.4 (*C*$(CH_3)_3$), 28.8 ($SO_2C(CH_3)_3$) and 24.2 (C(*C*$H_3)_3$); *m/z* [CI+(NH_3)] 281 (18%, MNH_4^+), 264 (15, MH^+), 246 (10), 206 (11), 169 (80), 155 (100), 144 (32), 126 (97), 112 (46), 100 (44), 94 (26), 86 (43) and 72 (67) (Found: MNH_4^+, 281.1898. $C_{12}H_{29}N_2O_3S$ requires 281.1899).

4.1.17. 2-Methyl-propane-2-sulfonic acid (2-hydroxy-3-phenyl-but-3-enyl)-amide 21. Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **13** (0.10 g, 0.49 mmol) in Et_2O (8 mL) was reacted with PhLi (1.50 mol dm^{-3} in light petroleum, 0.98 mL, 0.146 mmol). Column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **21** as a white solid (0.061 g, 44%); R_f 0.15 (40% Et_2O in petrol); mp 90.0–90.5°C; ν_{max} (KBr)/cm^{-1} 3479, 3305, 2983, 2936, 1691, 1632, 1600, 1479, 1450, 1398, 1367, 1306, 1229, 1208, 1126 and 1025; δ_H (400 MHz) 7.42–7.31 (5H, m, 5×H of Ar), 5.51 (1H, s, H of CH_2=), 5.47 (1H, s, H of CH_2=), 4.89 (1H, d, J=5.5 Hz, NH), 4.71–4.69 (1H, m, C*H*O), 3.44–3.38 (1H, m, H of CH_2N), 3.09–3.03 (1H, m, H of CH_2N), 2.95 (1H, br, s, OH) and 1.36 (9H, s, $C(CH_3)_3$); δ_C (100 MHz) 148.2 (*C*C=), 138.7 (C=), 128.6 (2×CH of Ar), 128.1 (CH of Ar), 126.5 (2×CH of Ar), 114.1 (CH_2=), 72.9 (CHO), 60.0 (*C*$(CH_3)_3$), 49.5 (CH_2N) and 24.2 (C(*C*$H_3)_3$); *m/z* [CI+(NH_3)] 301 (36%, MNH_4^+), 284 (24, MH^+), 169 (100), 152 (67), 131 (39), 119 (35) and 72 (20) (Found: MNH_4^+, 301.1578. $C_{14}H_{25}N_2O_3S$ requires 301.1586).

4.1.18. 2-Methyl-propane-2-sulfonic acid (2-hydroxy-3-methylene-pent-4-enyl)-amide 22. Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **13** (0.10 g, 0.49 mmol) in Et_2O (8 mL) was reacted with vinyllithium[26] (1.46 mol dm^{-3} in Et_2O, 1.0 mL, 1.46 mmol). Column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **22** as a white solid (0.060 g, 53%); R_f 0.21 (50% Et_2O in petrol); mp 87.5–88.5°C; ν_{max} (KBr)/cm^{-1} 3496, 3309, 2982, 2936, 2877, 1719, 1638, 1481, 1460, 1397, 1366, 1309, 1204, 1130, 1092, 1021 and 917; δ_H (400 MHz) 6.33 (1H, dd, J=18.0 Hz, 11.5, CH=), 5.40–5.38 (2H, m, H of CH_2=, H of C*H*$_2$=CH), 5.22 (1H, s, H of CH_2=), 5.13 (1H, d, J=11.5 Hz, H of C*H*$_2$=CH), 4.84–4.81 (1H, m, NH), 4.65–4.62 (1H, m, CHO), 3.52–3.47 (1H, m, H of CH_2N), 3.07–3.00 (1H, m, H of CH_2N), 1.38 (9H, s, $C(CH_3)_3$); δ_C (100 MHz) 145.8 (C=), 135.8 (CH=), 116.0 (*C*H_2=CH), 114.6 (CH_2=), 70.9 (CHO), 60.0 (*C*$(CH_3)_3$), 50.0 (CH_2N) and 24.2 (C(*C*$H_3)_3$); *m/z* [CI+(NH_3)] 251 (26%, MNH_4^+), 223 (100), 207 (14), 169 (12), 155 (37), 114 (10), 98 (12), 86 (16) and 52 (23) (Found: MNH_4^+, 251.1433. $C_{10}H_{23}N_2O_3S$ requires 251.1429).

4.1.19. 2-Methyl-propane-2-sulfonic acid (2-hydroxy-3-trimethylsilylmethyl-but-3-enyl)amide 24. Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **13** (0.10 g, 0.49 mmol) in Et_2O (8 mL) was reacted with $TMSCH_2Li$ (1.00 mol dm^{-3} in pentane, 1.46 mL, 1.46 mmol). Column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **24** as a white solid (0.099 g, 69%); R_f 0.16 (40% Et_2O in petrol); mp 83.5–84.0°C; (Found: C, 48.8; H, 9.6; N, 4.8. $C_{12}H_{27}NO_3$ SSi requires C, 49.1; H, 9.3; N, 4.8%); ν_{max} (KBr)/cm^{-1} 3436, 2955, 1480, 1420, 1366, 1306, 1249, 1159, 1126, 1094 and 1010; δ_H (400 MHz) 5.04 (1H, s, H of CH_2=), 4.80 (1H, s, H of CH_2=), 4.47–4.42 (1H, m, NH), 4.12–4.05 (1H, m, CHO), 3.46–3.40 (1H, m, H of CH_2N), 3.11–3.05 (1H, m, H of CH_2N), 1.66 (1H, d, J= 14.0 Hz, H of CH_2TMS), 1.42–1.35 (10H, m, $C(CH_3)_3$, H of CH_2TMS) and 0.05 (9H, s, TMS); δ_C (100 MHz) 146.6 (*C*=CH_2), 108.6 (CH_2=), 74.8 (CHOH), 60.0 (*C*$(CH_3)_3$), 48.9 (CH_2N), 24.3 (C(*C*$H_3)_3$), 23.0 (CH_2TMS) and −1.4 (TMS); *m/z* [CI+(NH_3)] 311 (100%, MNH_4^+), 294 (28, MH^+), 278 (16), 240 (22), 223 (60) and 210 (22) (Found: MNH_4^+, 311.1818. $C_{12}H_{31}N_2O_3$-SSi requires 311.1825).

4.1.20. 2-Methyl-propane-2-sulfonic acid (2-hydroxy-3-methylene-4-trimethylsilyl-nonyl)amide 23. Bu^{n}Li (2.30 mol dm^{-3} in hexane, 0.636 mL, 1.46 mmol) was added dropwise to a solution of trimethylvinylsilane (0.236 mL, 1.61 mmol) in THF (1 mL) at 0°C. After 1 h at 0°C the reaction was cooled to −78°C where upon a solution of *N*-Bus epoxide **13** (0.10 g, 0.49 mmol) in THF (8 mL) was added dropwise. After another 1 h at −78°C the reaction was warmed to 25°C for 1 h and then sat. aq. NH_4Cl (5 mL) was added. The reaction mixture was extracted with Et_2O (3×10 mL) and the combined organic extracts were washed with sat. aq. $NaHCO_3$ (15 mL), brine (15 mL), dried

($MgSO_4$) and evaporated under reduced pressure. Purification of the residue by column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **23** (2:1 mixture of diastereomers A:B) as a white solid (0.127 g, 72%); R_f 0.23 (50% Et_2O in petrol); mp 81.0–82.5°C; ν_{max} (KBr)/cm^{-1} 3562, 3353, 3000, 2995, 1501, 1466, 1403, 1398, 1352, 1256, 1163, 1102, 1001 and 964; δ_H (400 MHz) 5.18 (0.66H, s, H of CH_2= of B), 5.03 (0.33H, s, H of CH_2= of A), 4.99–4.92 (1H, m, NH), 4.75 (0.33H, s, H of CH_2= of A), 4.72 (0.66H, s, H of CH_2= of B), 4.06–4.04 (0.33H, m, CHO of A), 3.93 (0.66H, m, CHO of B), 4.50–4.42 (0.66H, m, H of CH_2N of B), 4.34–4.26 (0.33H, m, H of CH_2N of A), 3.13–3.04 (0.33H, m, H of CH_2N of A), 2.92–2.83 (0.66H, m, H of CH_2N of B), 2.80 (0.66H, br s, CHC= of B), 2.65 (0.33H, br s, CHC= of A), 1.65–1.42 (2H, m, CH_2CH_2CH), 1.37 (9H, s, $(CH_3)_3C$), 1.30–1.00 (6H, m, CH_2CH_3, CH_2CH, $CH_2CH_2CH_3$), 0.89–0.81 (3H, m, $CH_3(CH_2)_4$) and −0.03 (9H, s, TMS); δ_C (100 MHz) 151.3 (C=), 108.6 (CH_2= of A), 105.9 (CH_2= of B), 75.8 (CHO of A), 75.4 (CHO of B), 59.9 ($C(CH_3)_3$), 49.6 (CH_2N), 33.4 (CHC=), 31.1 (CH_2CH), 29.3 (CH_2CH_2CH), 28.7 ($CH_2CH_2CH_3$), 24.3 ($(CH_3)_3C$), 22.6 (CH_2CH_3), 14.1 (CH_3CH_2), −2.1 (TMS of A) and −2.8 (TMS of B); *m/z* [CI+(NH_3)] 381 (63%, MNH_4^+), 348 (23), 309 (19), 293 (17), 274 (20), 218 (24), 154 (100) and 90 (33) (Found: MNH_4^+, 381.2609. $C_{17}H_{41}N_2O_3SSi$ requires 381.2607).

4.1.21. *tert*-Butyl allyl(2-methylallyl)carbamate 26. Boc-protected allylamine **25** (2.00 g, 12.7 mmol) was added to a solution of NaH (0.42 g, 60% dispersion in mineral oil, 14 mmol) in DMF (100 mL) at ambient temperature. After 1 h the reaction was cooled to 0°C and methallyl bromide (1.41 mL, 14.0 mmol) was added. After 1 h the reaction was quenched with MeOH (10 mL) and then diluted with H_2O (70 mL) and washed with Et_2O (4×50 mL). The organic phases were combined, dried and the solvent removed to give a yellow oil. Purification of the residue by column chromatography (elution gradient 0–40% Et_2O in petrol) gave diene **26** (1:1 mixture of rotamers) as a clear colourless oil (2.55 g, 95%); R_f 0.71 (50% Et_2O in petrol); ν_{max} (film)/cm^{-1} 3080, 2976, 2927, 1699, 1657, 1478, 1456, 1406, 1366, 1244, 1173, 1144, 1098 and 1024; δ_H (400 MHz) 5.82–5.70 (1H, m, CH=), 5.17–5.06 (2H, m, CH_2=), 4.86 (1H, s, H of CH_2=), 4.74 (1H, s, H of CH_2=), 3.89–3.70 (4H, m, 2×NCH_2), 1.69 (3H, s, CH_3), and 1.48 (9H, s, $(CH_3)_3C$); δ_C (100 MHz) 155.6 (C=O), 142.4 (C=), 141.4 (C=), 133.8 (CH=), 116.6 (CH_2=), 116.1 (CH_2=), 111.5 (CH_2=), 79.5 ($C(CH_3)_3$), 51.5 (CH_2N), 48.6 (CH_2N), 48.2 (CH_2N), 28.3 ($(CH_3)_3C$) and 19.9 (CH_3); *m/z* [CI+(NH_3)] 212 (42%, MH^+), 173 (100), 156 (39), 152 (62), 112 (47), 98 (29), 95 (49), 81 (35) and 72 (24) (Found: MH^+, 212.1651. $C_{12}H_{22}NO_2$ requires 212.1650).

4.1.22. *tert*-Butyl 3-methyl-2,5-dihydropyrrole-1-carboxylic acid 28. Grubbs' 2nd generation catalyst[22] **27** (0.45 mg, 0.61 mmol) was added to a solution of diene **26** (2.55 g, 12.1 mmol) in anhydrous CH_2Cl_2 (750 mL) at reflux. The resulting mixture was stirred at reflux overnight, after which time TLC showed complete consumption of starting material (eluent 50% Et_2O in petrol). The reaction was quenched by exposure to air for ~2 h and the solvent was then removed under reduced pressure. Purification of the residue by column chromatography [elution gradient 0–30% Et_2O in petrol] gave alkene **28** (1:1 mixture of rotamers A and B) as a clear colourless oil (2.08 g, 94%); R_f 0.62 (50% Et_2O in petrol); ν_{max} (film)/cm^{-1} 3067, 2975, 2930, 2856, 2360, 2341, 1704, 1666, 1479, 1449, 1404, 1366, 1337, 1256, 1183, 1114 and 1019; δ_H (400 MHz) 5.47 (1H, br, d, *J*=19.0 Hz, CH=), 4.12–3.93 (4H, br, m, 2×CH_2N), 1.77 (1.5H, s, CH_3 of A), 1.74 (1.5H, s, CH_3 of B) and 1.51 (9H, s, $(CH_3)_3C$); δ_C (100 MHz) 154.2 (C=O), 135.3 (C=), 135.2 (C=), 119.4 (CH=), 119.3 (CH=), 79.1 ($C(CH_3)_3$), 79.0 ($C(CH_3)_3$), 56.3 (CH_2N), 55.9 (CH_2N), 53.4 (CH_2N), 53.1 (CH_2N), 28.5 (($CH_3)_3C$), and 19.9 (CH_3).

4.1.23. 1-Methyl-3-(2-methyl-propane-2-sulfonyl)-6-oxa-3-azabicyclo[3.1.0]hexane 29. Alkene **28** (0.50 g, 2.73 mmol) in CH_2Cl_2 (20 mL) was stirred with TFA (4.00 mL, 51.9 mmol) at room temperature for 4 h. The solvent was removed under reduced pressure and the residue co-evaporated with toluene (15 mL) to give the amine as a black oil (0.22 g, quant.); no other purification was required; ν_{max} (film)/cm^{-1} 3420, 2987, 2786, 2361, 2342, 1780, 1682, 1456, 1436, 1204, 1142, 1029 and 840; δ_H (400 MHz) 9.38 (2H, br s, NH_2), 5.47 (1H, s, CH=), 4.11 (2H, br, s, CH_2N), 3.98 (2H, br, s, CH_2N) and 1.84 (3H, s, CH_3); δ_C (100 MHz) 134.9 (=C), 118.1 (CH=), 54.5 (CH_2N), 52.4 (CH_2N), and 13.3 (CH_3); *m/z* [CI+NH_3] 82 (70%, MH^+), 80 (18), 69 (29), 68 (100), 67 (30), 55 (15), 45 (30) and 41 (31) (Found: MH^+, 82.0656. $C_5H_{10}N$ requires 82.0657).

To a solution of the above amine (0.22 g, 2.73 mmol) in CH_2Cl_2 (20 mL) at 25°C was added Et_3N (3.81 mL, 27.3 mmol) dropwise. After 1 h the reaction was cooled to 0°C and ice-cold *tert*-butylsulfinyl chloride[17] (0.767 g, 5.46 mmol) in CH_2Cl_2 (0.5 mL) was added. After 1 h (TLC monitoring, 30% Et_2O in petrol), the mixture was diluted with sat. aq. $NaHCO_3$ (30 mL). The aqueous layer was then extracted with CH_2Cl_2 (3×10 mL). The organic extracts were combined, dried ($MgSO_4$) and concentrated under reduced pressure to reveal a brown oil. Purification of the residue by column chromatography [elution gradient 0–40% Et_2O in petrol] gave the desired alkene as a clear colourless oil (0.501 g, 98%); R_f 0.56 (50% Et_2O in petrol); ν_{max} (film)/cm^{-1} 3424, 2985, 2714, 2509, 1680, 1476, 1394, 1300, 1203, 1180, 1135, 1030, and 801; δ_H (400 MHz) 5.38–5.32 (1H, m, CH=), 4.29–4.14 (2H, m, CH_2N), 3.97–3.87 (1H, m, H of CH_2N), 3.77–3.71 (1H, m, H of CH_2N), 1.74 (3H, br, s, CH_3C=) and 1.22 (9H, s, $(CH_3)_3C$); δ_C (100 MHz) 136.1 (=C), 120.2 (CH=), 68.1 ($C(CH_3)_3$), 57.4 (CH_2N), 55.8 (CH_2N), 23.0 ($C(CH_3)_3$) and 13.9 (CH_3).

1,1,1-Trifluoroacetone (3.56 mL, 39.8 mmol) was added dropwise to a stirred solution of the above alkene (0.501 g, 2.68 mmol) and aq. Na_2EDTA (4×10^{-4} mol dm^{-3}, 13.4 mL, 0.005 mmol) in MeCN (70 mL) at 0°C. A mixture of $NaHCO_3$ (1.80 g, 21.4 mmol) and Oxone® (8.24 g, 13.4 mmol) was then added portionwise over a period of 1 h. After 4 h, a mixture of $NaHCO_3$ (1.80 g, 21.4 mmol) and Oxone® (8.24 g, 13.4 mmol) was added and the reaction was stirred overnight. The reaction mixture was then diluted with water (50 mL), filtered and extracted with CH_2Cl_2 (3×50 mL). The combined organic extracts were

dried (Na_2SO_4) and concentrated under reduced pressure to give a yellow solid. Purification of the residue by column chromatography [elution gradient 0–60% Et_2O in petrol] gave epoxide **29** as a white solid (0.340 g, 58%); R_f 0.23 (50% Et_2O in petrol); mp 80.5–81.5°C; (Found: C, 48.9; H, 7.9; N, 6.4. $C_9H_{17}NO_3S$ requires C, 49.2; H, 7.8; N, 6.4%); ν_{max} (KBr)/cm^{-1} 2984, 1481, 1468, 1452, 1312, 1138, 1108, 1050 and 961; δ_H (400 MHz) 3.82 (1H, d, J=12.0 Hz, H of CH_2N), 3.73 (1H, d, J=11.5 Hz, H of CH_2N), 3.46–3.41 (2H, m, H of CH_2N, CHO), 3.34 (1H, d, J=11.5 Hz, H of CH_2N), 1.59 (3H, br, s, CH_3C=) and 1.39 (9H, s, $(CH_3)_3C$); δ_C (100 MHz) 77.2 (O*C*CH_3), 76.8 (*C*$(CH_3)_3$), 60.4 (CHO), 53.1 (CH_2N), 50.6 (CH_2N), 24.5 (C(*C*$H_3)_3$) and 15.1 (CH_3); *m/z* [CI+(NH_3)] 237 (100, MNH_4^+), 220 (12, MH^+), 124 (13), 110 (19), 100 (35), 84 (15), 69 (12), 58 (43), 52 (69) and 44 (94) (Found: MNH_4^+, 237.1269. $C_9H_{21}N_2O_3S$ requires 237.1273).

4.1.24. 2-Methyl-propane-2-sulfonic acid (2-hydroxy-2-methyl-3-methyleneheptyl)amide 30. Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **29** (0.10 g, 0.46 mmol) in Et_2O (8 mL) was reacted with Bu^{n}Li (1.60 mol dm^{-3} in pentane, 0.856 mL, 1.37 mmol). Column chromatography [elution gradient 30–100% Et_2O in petrol] gave amino alcohol **30** as a white solid (0.078 g, 62%); R_f 0.35 (50% Et_2O in petrol); mp 73.0–73.5°C; ν_{max} (KBr)/cm^{-1} 3492, 3302, 2958, 2932, 2873, 1722, 1640, 1480, 1459, 1397, 1366, 1308, 1208, 1126, 1086, 1022 and 953; δ_H (400 MHz) 5.19 (1H, s, H of CH_2=), 4.98 (1H, s, H of CH_2=), 4.44 (1H, t, J=5.5 Hz, NH), 3.20 (2H, d, J=5.5 Hz, CH_2N), 2.49 (1H, br, s, OH), 2.00 (2H, t, J=7.5 Hz, CH_2C=), 1.52–1.31 (16H, m, C*H*$_2$CH$_2$CH$_3$, C*H*$_2$CH$_3$, C$(CH_3)_3$, CH_3) and 1.93 (3H, t, J=7.0 Hz, C*H*$_3$(CH$_2$)$_3$); δ_C (100 MHz) 152.3 (C=), 109.7 (CH_2=), 75.1 (*C*$(CH_3)_3$), 60.0 (COH), 52.8 (CH_2N), 30.9 (*C*H_2C=), 30.6 (*C*$H_2CH_2CH_3$), 25.3 (*C*H_2CH_3), 24.3 (C(*C*$H_3)_3$), 22.6 (CH_3) and 14.0 (*C*H_3(CH$_2$)$_3$); *m/z* [CI+(NH_3)] 295 (98%, MNH_4^+), 262 (13), 261 (19), 260 (100), 204 (12), 158 (23), 140 (89) and 125 (20) (Found: MNH_4^+, 295.2056. $C_{13}H_{31}N_2O_3S$ requires 295.2055).

4.1.25. 2-Methyl-propane-2-sulfonic acid (2-hydroxy-2-methyl-3-phenylbut-3-enyl)amide 31. Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **29** (0.10 g, 0.46 mmol) in Et_2O (8 mL) was reacted with PhLi (1.80 mol dm^{-3} in hexane, 0.761 mL, 1.37 mmol). Column chromatography [elution gradient 30–100% Et_2O in petrol] gave amino alcohol **31** as a white solid (0.069 g, 51%); R_f 0.33 (50% Et_2O in petrol); mp 75.5–76.0°C; ν_{max} (KBr)/cm^{-1} 3451, 3295, 2986, 2937, 2875, 1480, 1454, 1442, 1425, 1396, 1376, 1307, 1207, 1162, 1120, 1094, 1077, 1026 and 960; δ_H (400 MHz) 7.38–7.30 (3H, m, H of Ar), 7.27–7.24 (2H, m, H of Ar), 5.59 (1H, s, H of CH_2=), 5.18 (1H, s, H of CH_2=), 4.51 (1H, br, t, J=6.0 Hz, NH), 3.37–3.26 (2H, m, CH_2N), 2.47 (1H, br, s, OH), 1.44 (3H, s, CH_3) and 1.35 (9H, s, C$(CH_3)_3$); δ_C (100 MHz) 153.4 (C=), 140.3 (C of Ar), 128.5 (CH of Ar), 128.2 (CH of Ar), 127.4 (CH of Ar), 115.8 (CH_2=), 74.6 (*C*$(CH_3)_3$), 60.0 (COH), 52.9 (CH_2N), 25.9 (CH_3), and 24.4 (C(*C*$H_3)_3$); *m/z* [CI+(NH_3)] 315 (100%, MNH_4^+), 280 (72), 178 (18), 166 (20), 164 (41), 160 (27), 145 (22) and 131 (12) (Found: MNH_4^+, 315.1740. $C_{15}H_{27}N_2O_3S$ requires 315.1742).

4.1.26. 2-Methyl-propane-2-sulfonic acid (2-hydroxy-2-methyl-3-(trimethylsilylmethyl)-but-3-enyl)amide 32. Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **29** (0.10 g, 0.46 mmol) in Et_2O (8 mL) was reacted with $TMSCH_2Li$ (1.0 mol dm^{-3} in light petroleum, 1.37 mL, 1.37 mmol). Column chromatography [elution gradient 30–100% Et_2O in petrol] gave amino alcohol **32** as a white solid (0.084 g, 60%); R_f 0.38 (50% Et_2O in petrol); mp 69.5–70.0°C; ν_{max} (KBr)/cm^{-1} 3497, 3306, 2987, 2955, 2898, 1629, 1480, 1458, 1420, 1396, 1366, 1309, 1248, 1168, 1127, 1082, 1022 and 941; δ_H (400 MHz) 5.01 (1H, s, H of CH_2=), 4.78 (1H, s, H of CH_2=), 4.43 (1H, t, J=6.0 Hz, NH), 3.21 (2H, d, J=6.0 Hz, CH_2N), 2.28 (1H, br, s, OH), 1.60 (1H, d, J=14.5 Hz, H of CH_2C=), 1.47 (1H, d, J=14.5 Hz, H of CH_2C=), 1.39 (9H, s, C$(CH_3)_3$), 1.32 (3H, s, CH_3) and 0.04 (9H, s, TMS); δ_C (100 MHz) 150.1 (C=), 108.9 (CH_2=), 75.2 (*C*$(CH_3)_3$), 59.9 (COH), 52.9 (CH_2N), 25.0 (CH_3), 24.3 (C(*C*$H_3)_3$), 21.1 (CH_2C=), and −0.79 (TMS); *m/z* [CI+(NH_3)] 325 (66%, MNH_4^+), 290 (29), 218 (75), 141 (22), 98 (100), 90 (49) and 52 (12) (Found: MNH_4^+, 325.1975. $C_{13}H_{33}N_2O_3SSi$ requires 325.1976).

4.1.27. *tert*-Butyl (3-hydroxy-4-methyleneoctyl)carbamate 34 and *tert*-butyl 4-hydroxy-3,4-dihydro-2*H*-pyridine-1-carboxylate 35. Following the general procedure for (2-Hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Boc epoxide **33**[23] (0.10 g, 0.50 mmol) in Et_2O (8 mL) was reacted with Bu^{n}Li (2.50 mol dm^{-3} in hexane, 0.603 mL, 1.51 mmol). Column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **34** as a clear colourless oil (0.009 g, 7%); R_f 0.33 (50% Et_2O in petrol); ν_{max} (film)/cm^{-1} 3375, 3083, 2959, 2952, 2873, 1693, 1601, 1516, 1456, 1427, 1392, 1367, 1304, 1278, 1251, 1224, 1171, 1110, 1066 and 1005; δ_H (400 MHz) 5.06 (1H, s, H of CH_2=), 4.92–4.79 (2H, m, H of CH_2=, NH), 4.16–4.08 (1H, m, CHO), 3.49–3.37 (1H, m, H of CH_2N), 3.18–3.13 (1H, m, H of CH_2N), 1.81–1.71 (1H, m, H of C*H*$_2$CHO), 2.15–1.93 (2H, m, CH_2C=), 1.66–1.17 (14H, m, H of C*H*$_2$CHO, C*H*$_2$CH$_2$ CH$_3$, $(CH_3)_3C$, C*H*$_2$CH$_3$) and 0.91 (3H, t, C*H*$_3$CH$_2$); δ_C (100 MHz) 156.0 (C=O), 151.8 (C=), 108.2 (CH_2=), 78.7 (*C*$(CH_3)_3$), 72.3 (CHO), 37.0 (CH_2N), 35.3 (*C*H_2CHO), 31.0 (CH_2C=), 29.7 (*C*H_2CH_2-CH_3), 27.7 ((*C*$H_3)_3$C), 21.9 (*C*H_2CH_3) and 13.0 (*C*H_3CH_2); *m/z* [CI+(NH_3)] 258 (23%, MH^+), 219 (20), 198 (32), 184 (23), 160 (19), 152 (29), 142 (56), 126 (32), 112 (53), 98 (100), 84 (65) and 72 (53) (Found: MH^+, 258.2069. $C_{14}H_{28}NO_3$ requires 258.2069). Also isolated was cyclic alcohol **35** as a clear colourless oil (0.080 g, 80%); R_f 0.11 (50% Et_2O in petrol); ν_{max} (film)/cm^{-1} 3466, 3055, 2978, 2993, 2878, 1694, 1644, 1477, 1456, 1414, 1367, 1306, 1267, 1242, 1168, 1122 and 1058; δ_H (400 MHz) 7.07–6.79 (1H, m, NCH=), 5.11–4.91 (1H, m, =C*H*CHO), 4.22–4.15 (1H, m, CHO), 3.95–3.75 (1H, m, H of CH_2N), 3.38–3.26 (1H, m, H of CH_2N), 1.99–1.73 (2H, m, C*H*$_2$CHO) and 1.65–1.14 (9H, m, $(CH_3)_3C$); δ_C (100 MHz) 158.2 (C=O), 127.6 (=CHN), 106.1 (=*C*HCHO), 79.9 (*C*$(CH_3)_3$), 60.5 (CHO), 37.2 (CH_2N), 30.2 (*C*H_2CHO) and 27.8 ((*C*$H_3)_3$C); *m/z* [CI+(NH_3)] 200 (27%, MH^+), 182 (69), 135 (25), 98

(22) and 82 (100) (Found: MH^+, 200.1286. $C_{10}H_{18}NO_3$ requires 200.1286).

4.1.28. 1-(2-Methyl-propane-2-sulfinyl)-1,2,3,6-tetrahydropyridine 37. Et_3N (16.8 mL, 120 mmol) was added to a solution of 1,2,3,6-tetrahydropyridine **36** (1.00 g, 12 mmol) in CH_2Cl_2 (100 mL) at 25°C. The reaction was allowed to stir for 1 h before *tert*-butylsulfinyl chloride[17] (3.39 g, 24 mmol) in CH_2Cl_2 (5 mL) was added to the mixture at 0°C. After 4 h (TLC monitoring, 30% Et_2O in petrol), the mixture was diluted with sat. aq. $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3×30 mL). The organic extracts were combined, dried ($MgSO_4$) and concentrated under reduced pressure. Purification of the residue by column chromatography [elution gradient 0–30% Et_2O in petrol] gave alkene **37** as a clear colourless oil (2.16 g, 96%); R_f 0.61 (50% Et_2O in petrol); ν_{max} (film)/cm^{-1} 3034, 2955, 2921, 2865, 2836, 1657, 1590, 1476, 1458, 1432, 1388, 1362, 1300, 1231, 1205, 1108, 1079, 1040 and 1005; δ_H (400 MHz) 5.81–5.74 (1H, m, NCH_2CH=), 5.69–5.61 (1H, m, CH=), 3.72–3.61 (1H, m, H of NCH_2CH), 3.59–3.50 (1H, m, H of NCH_2CH=), 3.43–3.34 (1H, m, H of CH_2CH_2CH=), 3.27–3.17 (1H, m, H of CH_2CH_2CH=), 2.19–2.17 (2H, br, m, NCH_2CH_2) and 1.16 (9H, s, $(CH_3)_3C$); δ_C (100 MHz) 125.7 (NCH_2CH=), 124.8 (CH=), 58.2 ($C(CH_3)_3$), 44.6 (NCH_2CH=), 44.1 (CH_2CH_2CH=), 25.5 (NCH_2CH_2) and 23.2 ($(CH_3)_3C$); *m/z* [CI+(NH_3)] 205 (20%, MNH_4^+), 188 (100, MH^+), 172 (18), 114 (10), 98 (19), 84 (52) and 82 (65) (Found: MH^+, 188.1111. $C_9H_{18}NOS$ requires 188.1109).

4.1.29. 3-(2-Methyl-propane-2-sulfonyl)-7-oxa-3-aza-bicyclo[4.1.0]heptane 38. *m*CPBA (9.91 g, 28.7 mmol, 50% *w/w* in H_2O) was added to a solution of alkene **37** (1.92 g, 10.3 mmol) in CH_2Cl_2 (200 mL) at 25°C. After 1 h the reaction was complete (TLC) and was quenched by addition of 10% aq. sodium bisulfite solution until all the oxidant had been consumed (starch iodide paper). The organic layer was separated and washed with sat. aq. $NaHCO_3$ and brine, the extract was dried ($MgSO_4$) and solvent removed to give a yellow oil. Purification of the residue by column chromatography [elution 40%–100% Et_2O in petrol] gave epoxide **38** as a white crystalline solid (1.62 g, 72%); R_f 0.21 (60% Et_2O in petrol); mp 88.0–88.5°C; (Found: C, 49.3; H, 7.8; N, 6.3. $C_9H_{17}NO_3S$ requires C, 49.3; H, 7.8; N, 6.4%); ν_{max} (KBr)/cm^{-1} 3000, 2983, 2940, 2920, 2876, 1480, 1453, 1426, 1397, 1366, 1308, 1257, 1181, 1158, 1121, 1093, 1070, 1047 and 1020; δ_H (400 MHz) 3.93 (1H, d, *J*=14.0 Hz, H of $CHCH_2N$), 3.63 (1H, d, *J*=14.0 Hz, H of $CHCH_2N$), 3.31–3.15 (4H, m, NCH_2CHO, $N(CH_2)_2CHO$, CH_2CH_2N), 2.23–2.01 (2H, m, CH_2CH_2N) and 1.34 (9H, s, $(CH_3)_3C$); δ_C (100 MHz) 60.8 ($C(CH_3)_3$), 50.0 (CHO), 49.7 (CHO), 45.0 ($CHCH_2N$), 40.6 (CH_2CH_2N), 24.9 (CH_2CH_2N) and 23.8 ($(CH_3)_3C$); *m/z* [CI+(NH_3)] 237 (100%, MNH_4^+), 220 (26, MH^+) and 100 (27) (Found: MNH_4^+, 237.1271. $C_9H_{21}N_2O_3S$ requires 237.1273).

4.1.30. 2-Methyl-propane-2-sulfonic acid (3-hydroxy-4-methyleneoctyl)amide 39 (R=Bu^n) and 1-(2-methyl-propane-2-sulfonyl)-1,2,3,4-tetrahydropyridin-4-ol 40. Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **38** (0.10 g, 0.46 mmol) in Et_2O (8 mL) was reacted with Bu^{n}Li (2.50 mol dm^{-3} in light petroleum, 0.548 mL, 1.37 mmol). Column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **39** (R=Bu^n) as a white solid (0.065 g, 51%); R_f 0.31 (50% Et_2O in petrol); mp 76.0–76.5°C; ν_{max} (film)/cm^{-1} 3480, 3295, 2932, 2873, 1705, 1647, 1480, 1456, 1366, 1303, 1207, 1126, 1088 and 1021; δ_H (400 MHz) 5.09 (1H, s, H of CH_2=), 4.89 (1H, s, H of CH_2=), 4.84–4.75 (1H, m, NH), 4.29–4.22 (1H, m, CHO), 2.64–2.59 (2H, m, CH_2N), 2.32–2.22 (1H, m, OH), 2.08 (1H, dt, *J*=16.0, 8.0 Hz, H of CH_2C=), 1.99 (1H, dt, *J*=16.0, 8.0 Hz, H of CH_2C=), 1.90–1.80 (1H, m, H of CH_2CHO), 1.78–1.67 (1H, m, H of CH_2CHO), 1.49–1.26 (13H, m, $(CH_3)_3C$, $CH_2CH_2CH_3$, CH_2CH_3) and 0.90 (3H, t, *J*=7.5 Hz, CH_2CH_3); δ_C (100 MHz) 151.5 (C=), 109.2 (CH_2=), 73.5 (CHO), 59.8 ($C(CH_3)_3$), 42.3 (CH_2N), 35.9 (CH_2CHO), 31.5 (CH_2CH=), 30.1 ($CH_2CH_2CH_3$), 24.3 ($(CH_3)_3C$), 22.7 (CH_2CH_3), and 14.0 (CH_3); *m/z* [CI+(NH_3)] 295 (100%, MNH_4^+), 278 (40, MH^+), 260 (18), 204 (12), 186 (10), 158 (23), and 140 (94) (Found: MNH_4^+, 295.2057. $C_{13}H_{31}N_2O_3S$ requires 295.2055). Also isolated was cyclic alcohol **40** as a clear colourless oil (0.017 g, 17%); R_f 0.13 (50% Et_2O in petrol); ν_{max} (film)/cm^{-1} 3506, 2976, 2935, 2884, 2257, 1641, 1481, 1463, 1397, 1366, 1324, 1272, 1205, 1138, 1079, 1050, 1020 and 996; δ_H (400 MHz) 6.61 (1H, d, *J*= 8.0 Hz, NCH=), 5.07–4.97 (1H, m, CH=), 4.22–4.13 (1H, m, CHOH), 3.88–3.77 (1H, m, H of NCH_2), 3.45 (1H, dt, *J*=12.0, 3.0 Hz, H of NCH_2), 2.30–2.18 (1H, m, OH), 2.00–1.75 (2H, br, m, CH_2CHOH) and 1.39 (9H, s, $(CH_3)_3C$); δ_C (100 MHz) 129.3 (NCH=), 105.9 (CH=), 62.1 (CHOH), 59.7 ($C(CH_3)_3$), 41.6 (NCH_2), 30.9 (CH_2CHOH), and 24.5 ($(CH_3)_3C$); *m/z* [CI+(NH_3)] 237 (70%, MNH_4^+), 220 (10, MH^+), 140 (12), 99 (27), 98 (32), 82 (55), 80 (47), 70 (14) and 57 (100) (Found: MNH_4^+, 237.1272. $C_9H_{21}N_2O_3S$ requires 237.1273).

4.1.31. 2-Methyl-propane-2-sulfonic acid (3-hydroxy-5-methyl-4-methylenehexyl)amide 39 (R=Pr^i). Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **38** (0.10 g, 0.46 mmol) in Et_2O (8 mL) was reacted with Pr^{i}Li (2.00 mol dm^{-3}in light petroleum, 0.685 mL, 1.37 mmol). Column chromatography [elution gradient 30–100% Et_2O in petrol] gave amino alcohol **39** (R=Pr^i) as a white solid (0.028 g, 23%); R_f 0.34 (50% Et_2O in light Petroleum); mp 96.0–96.5°C; ν_{max} (KBr)/cm^{-1} 3498, 3295, 2962, 2934, 2874, 1647, 1480, 1459, 1396, 1366, 1304, 1206, 1127, 1096 and 902; δ_H (400 MHz) 5.09 (1H, s, H of CH_2=), 4.98 (1H, s, H of CH_2=), 4.77 (1H, t, *J*=5.0 Hz, NH), 4.30–4.28 (1H, m, CHO), 3.46–3.24 (2H, m, CH_2N), 2.23 (1H, septet, *J*=7.0 Hz, CHC=), 1.91–1.83 (1H, m, H of CH_2CHO), 1.79–1.68 (1H, m, H of CH_2CHO), 1.42 (9H, s, $(CH_3)_3C$)), 1.09 (3H, d, *J*=7.0 Hz, CH_3CH) and 1.05 (3H, d, *J*=7.0 Hz, CH_3CH); δ_C (100 MHz) 158.5 (C=), 107.2 (CH_2=), 72.7 ($C(CH_3)_3$), 59.7 (CHO), 42.5 (CH_2N), 36.4 (CH_2CHOH), 30.4 (CHC=), 24.3 ($(CH_3)_3C$), 23.2 (CH_3CH) and 22.4 (CH_3CH); *m/z* [CI+(NH_3)] 281 (23%, MNH_4^+), 264 (27, MH^+), 246 (13), 183 (15), 155 (44), 144 (33), 128 (100), 126 (22), 110 (10), 98 (13), 90 (10), 82 (15), 72 (10), 58 (69) and 44 (69) (Found: MNH_4^+, 281.1898. $C_{12}H_{29}N_2O_3S$ requires 281.1899).

4.1.32. 2-Methyl-propane-2-sulfonic acid (3-hydroxy-5-methyl-4-methyleneheptyl)amide 39 (R=Bu^s). Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **38** (0.10 g, 0.46 mmol) in Et_2O (8 mL) was reacted with Bu^{s}Li (1.20 mol dm^{-3} in light petroleum, 1.14 mL, 1.37 mmol). Column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **39** (R=Bu^s, 1:1 mixture of diastereomers A:B) as a white solid (0.052 g, 41%); R_f 0.33 (50% Et_2O in petrol); mp 78.5–79.0°C; ν_{max} (KBr)/cm^{-1} 3489, 3295, 3088, 2963, 2633, 2875, 1646, 1480, 1456, 1422, 1396, 1366, 1304, 1207, 1127, 1090, 1022 and 955; δ_H (400 MHz) 5.11 (1H, d, *J*=6.5 Hz, H of CH_2=), 4.89 (1H, d, *J*=6.5 Hz, H of CH_2=), 4.85–4.79 (1H, m, NH), 4.27–4.20 (1H, m, CHO), 3.41–3.25 (2H, m, CH_2N), 2.30–2.15 (1H, m, OH), 2.04–1.94 (1H, m, CHC=), 1.93–1.82 (1H, m, CH_2CHO of A), 1.78–1.65 (1H, m, CH_2CHO of B), 1.56–1.30 (11H, m, $(CH_3)_3C$, CH_2CH_3), 1.07 (1.5H, d, *J*=7.0 Hz, CHCH_3 of A), 1.03 (1.5H, d, *J*=7.0 Hz, CHCH_3 of B), 0.87 (1.5H, t, *J*=6.5 Hz, CH_2CH_3 of A) and 0.84 (1.5H, t, *J*=6.5 Hz, CH_2CH_3 of B); δ_C (100 MHz) 157.3 (C= of A), 157.2 (C= of B), 107.9 (CH_2= of A), 107.8 (CH_2= of B), 73.2 (CHO of A), 72.9 (CHO of B), 59.7 ($C(CH_3)_3$), 42.5 (CH_2N of A), 42.4 (CH_2N of B), 37.6 (*C*HC= of A), 37.3 (*C*HC= of B), 36.4 (*C*H_2CHO of A), 36.3 (*C*H_2CHO of B), 29.8 (*C*H_2CH_3 of A), 28.9 (*C*H_2CH_3 of B), 24.3 ((*C*H_3)$_3$C of A), 24.1 ((*C*H_3)$_3$C of B), 21.3 (CH*C*H_3 of A), 20.2 (CH*C*H_3 of B), 12.0 (CH_2*C*H_3 of A) and 11.8 (CH_2*C*H_3 of B); *m/z* [CI+(NH_3)] 295 (100%, MNH_4^+), 278 (24, MH^+), 260 (14), 158 (12), 142 (19) and 140 (100) (Found: MNH_4^+, 295.2057. $C_{13}H_{31}N_2O_3S$ requires 295.2055).

4.1.33. 2-Methyl-propane-2-sulfonic acid (3-hydroxy-5,5-dimethyl-4-methylenehexyl)amide 39 (R=Bu^t). Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **38** (0.10 g, 0.46 mmol) in Et_2O (8 mL) was reacted with ^{t}BuLi (1.70 mol dm^{-3} in hexane, 0.806 mL, 1.37 mmol). Column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **39** (R=^{t}Bu) as a white solid (0.057 g, 45%); R_f 0.31 (50% Et_2O in petrol); mp 80.0–80.5°C; ν_{max} (KBr)/cm^{-1} 3488, 3295, 2967, 2875, 1638, 1481, 1465, 1421, 1397, 1364, 1303, 1202, 1127, 1089, 1022 and 961; δ_H (400 MHz) 5.18 (1H, s, H of CH_2=), 5.05 (1H, s, H of CH_2=), 4.84–4.77 (1H, m, NH), 4.42–4.37 (1H, m, CHO), 3.45 (1H, dt, *J*=11.0, 7.0 Hz, H of CH_2N), 3.33 (1H, d, *J*=11.0, 7.0 Hz, H of CH_2N), 1.99–1.91 (1H, br, m, OH), 1.87–1.78 (2H, m, CH_2CHO), 1.40 (9H, s, $(CH_3)_3CS$), and 1.10 (9H, s, $(CH_3)_3C$); δ_C (100 MHz) 161.8 (C=), 108.2 (CH_2=), 69.0 (CHO), 65.8 ($C(CH_3)_3$), 59.7 (S*C*$(CH_3)_3$), 43.0 (CH_2N), 39.1 (*C*H_2CHO), 29.2 ((*C*H_3)$_3$C), and 24.3 ((*C*H_3)$_3$CS); *m/z* [CI+(NH_3)] 295 (95%, MNH_4^+), 278 (39, MH^+), 277 (21), 260 (14), 142 (40) and 140 (100) (Found: MNH_4^+, 295.2054. $C_{13}H_{31}N_2O_3S$ requires 295.2054).

4.1.34. 2-Methyl-propane-2-sulfonic acid (3-hydroxy-4-phenyl-pent-4-enyl)amide 39 (R=Ph). Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **38** (0.10 g, 0.46 mmol) in Et_2O (8 mL) was reacted with PhLi (1.80 mol dm^{-3} in light petroleum, 0.761 mL, 1.37 mmol). Column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **39** (R=Ph) as a white solid (0.007 g, 5%); R_f 0.31 (50% Et_2O in petrol); mp 78.5–79.0°C; ν_{max} (KBr)/cm^{-1} 3302, 2926, 1641, 1452, 1366, 1305, 1126, 1082, 1020 and 952; δ_H (400 MHz) 7.40–7.28 (5H, m, Ar), 5.43 (1H, s, H of CH_2=), 5.37 (1H, s, H of CH_2=), 4.91–4.86 (1H, br, m, NH), 4.53–4.49 (1H, m, CHO), 3.46–3.38 (1H, m, H of CH_2N), 3.34–3.25 (1H, m, H of CH_2N), 2.30 (1H, br, s, OH), 1.93–1.82 (1H, m, H of CH_2CHO), 1.74–1.66 (1H, m, H of CH_2CHO), and 1.41 (9H, s, $(CH_3)C$); δ_C (100 MHz) 151.1 (*C*C=), 139.3 (C=), 128.4 (2×CH of Ar), 127.8 (CH of Ar), 126.7 (2×CH of Ar), 112.7 (CH_2=), 65.7 (CHOH), 59.7 ($C(CH_3)_3$), 42.1 (CH_2N), 36.0 (*C*H_2CHOH), and 24.3 ((*C*H_3)$_3$C); *m/z* [CI+(NH_3)] 315 (86%, MNH_4^+), 298 (43, MH^+), 202 (25), 180 (52), 178 (84), 176 (37), 162 (70), 160 (100), 152 (51), 146 (24), 145 (22), 120 (20), 100 (21), 98 (32), 86 (25), 84 (42), 72 (27) and 61 (28) (Found: MNH_4^+, 315.1746. $C_{15}H_{27}N_2O_3S$ requires 315.1742).

4.1.35. 2-Methyl-propane-2-sulfonic acid (3-hydroxy-4-trimethylsilanylmethyl-pent-4-enyl)amide 39 (R=CH_2TMS). Following the general procedure for (2-hydroxy-3-methylene-heptyl)-carbamic acid *tert*-butyl ester **10a**, *N*-Bus epoxide **38** (0.10 g, 0.46 mmol) in Et_2O (8 mL) was reacted with $TMSCH_2Li$ (1.00 mol dm^{-3} in pentane, 1.37 mL, 1.37 mmol). Column chromatography [elution gradient 30–60% Et_2O in petrol] gave amino alcohol **39** (R=CH_2TMS) as a white solid (0.060 g, 43%); R_f 0.32 (50% Et_2O in petrol); mp 72.5–73.0°C; ν_{max} (KBr)/cm^{-1} 3492, 3295, 2954, 1638, 1480, 1454, 1421, 1366, 1303, 1249, 1205, 1127, 1087 and 853; δ_H (400 MHz) 4.97 (1H, s, H of CH_2=), 4.79 (1H, br, t, *J*=6.0 Hz, NH), 4.70 (1H, s, H of CH_2=), 4.11–4.07 (1H, m, CHO), 2.67–2.63 (2H, m, CH_2N), 2.26–2.21 (1H, br, m, OH), 1.96–1.82 (1H, m, H of CH_2CHO), 1.76–1.66 (1H, m, H of CH_2CHO), 1.62 (1H, d, *J*=14.0 Hz, H of CH_2TMS), 1.41–1.32 (11H, m, $(CH_3)C$, H of CH_2TMS), and 0.03 (3H, s, TMS); δ_C (100 MHz) 149.3 (C=), 107.2 (CH_2=), 74.0 (CHO), 59.7 ($C(CH_3)_3$), 42.2 (CH_2N), 35.8 (*C*H_2CHO), 24.3 ((*C*H_3)$_3$C), 22.6 (CH_2TMS) and −1.3 (TMS); *m/z* [CI+(NH_3)] 325.2 (35%, MNH_4^+), 170.1 (22) and 98.1 (100) (Found: MNH_4^+, 325.1983. $C_{13}H_{33}N_2O_3SiS$ requires 325.1981).

Acknowledgements

We thank the EPSRC for a research grant (GR/M72340) and GlaxoSmithKline for a CASE award (to T. J. M.). We also thank the EPSRC National Mass Spectrometry Service Centre for mass spectra.

References

1. Erden, I. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon Press: Oxford, 1996; Vol. 1A, pp 97–171.
2. (a) Crandall, J. K.; Lin, L.-H. C. *J. Am. Chem. Soc.* **1967**, *89*, 4526–4527. (b) Crandall, J. K.; Lin, L.-H. C. *J. Am. Chem. Soc.* **1967**, *89*, 4527–4528. (c) Crandall, J. K.; Apparu, M. *Org. React. (N. Y.)* **1983**, *29*, 345–443.

3. (a) Satoh, T. *Chem. Rev.* **1996**, *96*, 3303–3325. (b) Doris, E.; Dechoux, L.; Mioskowski, C. *Synlett* **1998**, 337–345. (c) Hodgson, D. M.; Gras, E. *Synthesis* **2002**, 1625–1642. (d) Hodgson, D. M.; Gras, E.; Tomooka, K. In *Organolithiums in Enantioselective Synthesis, Topics in Organometallic Chemistry*; Hodgson, D. M., Ed.; Springer: Berlin, 2003; Vol. 5, pp 217–250.
4. (a) Hodgson, D. M.; Stent, M. A. H.; Wilson, F. X. *Org. Lett.* **2001**, *3*, 3401–3403. (b) Hodgson, D. M.; Stent, M. A. H.; Wilson, F. X. *Synthesis* **2002**, 1445–1453.
5. (a) Hodgson, D. M.; Maxwell, C. R.; Miles, T. J.; Paruch, E.; Stent, M. A. H.; Matthews, I. R.; Wilson, F. X.; Witherington, J. *Angew. Chem., Int. Ed.* **2002**, *41*, 4313–4316, corrigendum, 4611. (b) Hodgson, D. M.; Stent, M. A. H.; Stefane, B.; Wilson, F. X. *Org. Biomol. Chem.* **2003**, *1*, 1139–1150.
6. (a) Kocienski, P.; Barber, C. *Pure Appl. Chem.* **1990**, *62*, 1933–1940. (b) Kasatkin, A. N.; Whitby, R. J. *Tetrahedron Lett.* **2000**, *41*, 5275–5280.
7. Preliminary communication: Hodgson, D. M.; Miles, T. J.; Witherington, J. *Synlett* **2002**, 310–312.
8. (a) Bergmeier, S. C. *Tetrahedron* **2000**, *56*, 2561–2576. (b) Kunieda, T.; Ishizuka, T. In *Studies in Natural Product Chemistry*; Rahman, A., Ed.; Elsevier: Amsterdam, 1993; Vol. 12, pp 411–445. (c) Ager, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 835–875.
9. Beak, P.; Kerrick, S. T.; Wu, S. D.; Chu, J. X. *J. Am. Chem. Soc.* **1994**, *116*, 3231–3239.
10. Allylic alkoxide **5** (Scheme 2) could also form from α-lithiatated epoxide via adjacent C–H insertion. For examples of this process giving allylic alcohols from cyclopentene epoxide, see: (a) Hodgson, D. M.; Gibbs, A. R.; Drew, M. G. B. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3579–3590. (b) Morgan, K. M.; Gronert, S. *J. Org. Chem.* **2000**, *65*, 1461–1466.
11. Hansen, S. U.; Bols, M. *Acta Chem. Scand.* **1998**, *52*, 1214–1222.
12. (a) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2039–2041. (b) Fu, G. C.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1993**, *115*, 9856–9857. (c) Ferguson, M. L.; O'Leary, D. J.; Grubbs, R. H. *Org. Synth.* **2003**, *80*, 85–92.
13. Sturmer, R.; Schafer, B.; Wolfart, V.; Stahr, H.; Kazmaier, U.; Helmchen, G. *Synthesis* **2001**, 46–48.
14. Tsuzuki, Y.; Chiba, K.; Mizuno, K.; Tomita, K.; Suzuki, K. *Tetrahedron: Asymmetry* **2001**, *12*, 2989–2997.
15. Yang, D.; Wong, M. K.; Yip, Y. C. *J. Org. Chem.* **1995**, *60*, 3887–3889.
16. (a) Hodgson, D. M.; Robinson, L. A. *Chem. Commun.* **1999**, 309–310. (b) Hodgson, D. M.; Cameron, I. D.; Christlieb, M.; Green, R.; Lee, G. P.; Robinson, L. A. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2161–2174.
17. Sun, P.; Weinreb, S. M.; Shang, M. *J. Org. Chem.* **1997**, *62*, 8604–8608.
18. Gontacharov, A. V.; Liu, H.; Sharpless, K. B. *Org. Lett.* **1999**, *1*, 783–786.
19. Fleming, I.; Dunoguès, J.; Smithers, R. *Org. React. (N. Y.)* **1989**, *37*, 57–575.
20. Ager, D. J. *Org. React. (N. Y.)* **1990**, *38*, 1–223.
21. Kirkland, T. A.; Grubbs, R. H. *J. Org. Chem.* **1997**, *7310*, 7318.
22. (a) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953–956. (b) Chatterjee, A. K.; Morgan, J. P.; Scholl, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 3783–3784.
23. Zhao, S.; Ghosh, A.; D'Andrea, S.; Freeman, J. P.; VonVoigtlander, P. F.; Carter, D. B.; Smith, M. W.; Blinn, J. R.; Szmuszkovicz, J. *Heterocycles* **1994**, *39*, 163–170.
24. Hodgson, D. M.; Gibbs, A. R.; Lee, G. P. *Tetrahedron* **1996**, *52*, 14361–14384.
25. Sukeda, M.; Ichikawa, S.; Matsuda, A.; Shuto, S. *J. Org. Chem.* **2003**, *68*, 3465–3475.
26. Seyferth, D.; Weiner, M. A. *J. Am. Chem. Soc.* **1961**, *83*, 3583–3586.