Regiochemical switching of Mitsunobu cyclisation mode of vicinal diamines with pendant hydroxyl group

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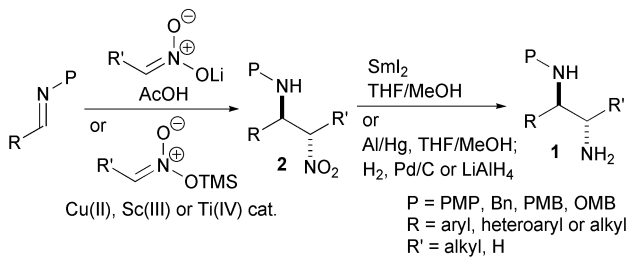
Ambident 1,2-diamines derived from the nitro-Mannich reaction containing both a tosyl amide and a secondary amine could be regioselectively cyclised through the tosyl amide onto a pendant primary hydroxyl group to give piperazine (60–75% yields) or 1,4-diazepane (71% yield) ring systems under Mitsunobu conditions. For some substrates addition of $Et_3N{\cdot}HCl$ encouraged regioselective cyclisation through the secondary amine leading to aziridine ring systems.

Introduction

We have developed the classic nitro-Mannich reaction,[1] for the stereoselective synthesis of 1,2-diamines **1** *via* the reduction of β-nitroamines **2** (Scheme 1).[2,3] Both the AcOH-promoted addition of nitronate anions, and the Lewis acid catalysed addition of preformed silyl nitronates, to aldimines is highly diastereoselective for a number of aryl, heteroaryl and alkyl imines.[4] The latter process has been made enantioselective by the use of a chiral ^{t}Bu-BOX Cu(II) catalyst.[5] Many other groups have also developed diastereo- and enantioselective nitro-Mannich reactions since our first contribution to this area.[6,7]



Scheme 1 Stereoselective synthesis of 1,2-diamines using the nitro-Mannich reaction.

The use of β-nitroamines as building blocks for heterocyclic synthesis has only briefly been investigated, probably due to the propensity of this class of molecule toward β-elimination.[8,2] In an early isolated example of the nitro-Mannich reaction, intramolecular cyclisation of the amino function of a racemic β-nitroamine onto a pendant ester formed a 2-oxopiperidine.[9] Shibasaki *et. al.* demonstrated the intramolecular cyclisation of an enantiomerically pure β-nitroamine onto a pendant aldehyde to give a piperidine.[10] We have begun to investigate the more stable 1,2-diamine products, derived from the β-nitroamine products of the nitro-Mannich reaction, as stereodefined building blocks in organic synthesis, particularly to access heterocyclic systems. An inherent problem of this approach is the ambident nucleophile character of 1,2-diamines. Initially we have looked at the *N*-susbtituent (P, Fig. 1) of the imine partner in the nitro-Mannich reaction to give cyclisation precursor **3**, after reduction of the nitro function, to investigate cyclisation mode 'a' (Fig. 1). In this paper we report our investigation into inducing this type of cyclisation and the eventual discovery that the Mitsunobu reaction can be used to access either cyclisation mode 'a' or 'b' (Fig. 1) from the pendant hydroxyl compound ($P = (CH_2)_2OH$).

Fig. 1 Possible cyclisation modes.

Results and discussion

The most common methods of synthesising heterocyclic compounds involve cyclisation *via* condensation or displacement of a leaving group. We envisaged that piperazine derivatives **4** could be accessed from either pendant carbonyl derivatives **5** or pendant leaving groups **6** (Fig. 2). Both of these strategies could be accessible from pendant alkene **7** or pendant alcohol **8**.

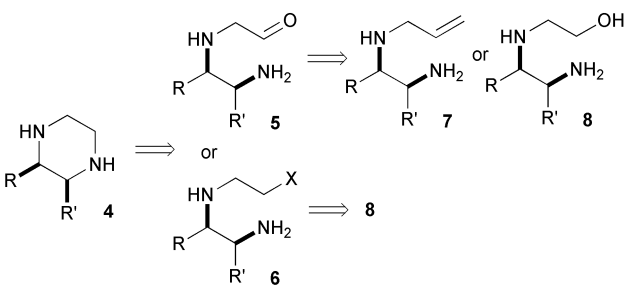


Fig. 2 Retrosynthetic access to cyclic systems.

Synthesis of **7** (R = Ph, R′ = Et) was straightforward,[3] but attempts at interconversion of the alkene to a carbonyl group failed to give any desired product under a variety of oxidation systems.[11] In addition direct electrophile induced cyclisation[12] or

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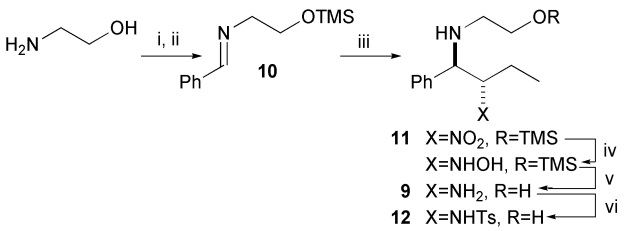
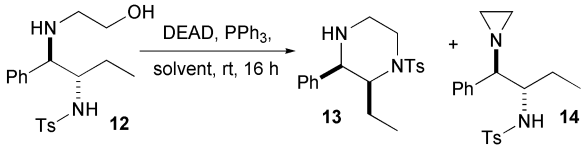
more exotic amination reactions[13] also failed. The presence of both of the amine functions seemed to be deleterious in one way or another to the desired reactions and this was not alleviated by tosyl protection of the primary amine in **7**.

Synthesis of the pendant hydroxyl compound **9** (**8**, R = Ph, R′ = Et) began with TMS protection of 2-aminoethanol followed by condensation with benzaldehyde to give imine **10** (Scheme 2). An AcOH promoted nitro-Mannich reaction of **10** with the lithium nitronate of nitropropane proceeded in good yield and diastereoselectivity (87%, dr >95 : 5 by ^{1}H NMR). The stereochemistry was assigned by analogy to previous examples that have been correlated by single X-ray crystallography.[2,4,5] Diamine **9** was then accessed using our more efficient reduction protocol involving reduction of the nitro function to the hydroxylamine with Al–Hg amalgam followed by $LiAlH_4$ reduction of the crude material to give a 71% yield of diastereomerically pure **9** over 2 steps. The TMS group was conveniently lost in the $LiAlH_4$ step.[14]



Scheme 2 *Reagents and conditions*: i, TMSCl, DMAP, Et_3N, CH_2Cl_2, −15 °C then rt, 16 h, 88% crude, ii, PhCHO, CH_2Cl_2, 4 Å MS, rt, 16 h, 81% crude, iii, 1-nitropropane, *n*-BuLi, THF, −78 °C, 10 min, AcOH, −78 °C then rt, 30 min, 87%; iv, Al–Hg, MeOH, THF, 5 °C then rt, 1 h, v, $LiAlH_4$, Et_2O, 0 °C then rt, 16 h, 71% over 2 steps, vi, TsCl, Et_3N, THF, rt, 16 h, 75%.

Attempted oxidation of the pendant hydroxyl group of **9** using mild oxidation systems which are known to avoid over oxidation of β-amino alcohols (SO_3–pyridine or PCC), gave only degradation.[15,16] Simple activation of the hydroxyl group as a tosyl ester was attempted from the sodium alkoxide, but led to intractable mixtures of *N*-tosylated primary amine, tertiary aziridine, pendant $–CH_2CH_2Cl$ and degradation. Reluctantly we turned to the Mitsunobu reaction[17] which has been shown to be useful for the synthesis of heterocycles from *N*-Ts amides.[18] Treatment of the unprotected substrate **9** with DEAD and triphenylphosphine was attempted, but in line with the lack of literature precedent gave an inseparable mixture of complex products. Protection of the primary amine as an *N*-Ts amide was achieved by standard means to give **12** in 75% yield (Scheme 2). Initial investigation into the Mitsunobu cyclisation of **12** using DEAD gave rise to the desired piperazine **13** in a moderate 60% yield [eqn (1)]. In an attempt to optimise this reaction, repetition with a different batch of **12** then gave rise to the aziridine **14** [eqn (1)].[19] After some control experiments we reasoned that traces of $Et_3N{\cdot}HCl$ in the starting material **12** from the previous tosylation reaction was altering the mode of cyclisation. This was present despite a workup involving an aqueous wash with satd. aq. $NaHCO_3$ solution. The effect of $Et_3N{\cdot}HCl$ was then investigated in the Mitsunobu cyclisation of **12** [eqn (1), Table 1].



(1)

Traces of $Et_3N{\cdot}HCl$ could be completely removed from tosylate **12** by a base wash (1 M aq. NaOH) of the crude material before purification by column chromatography. Cyclisation of this material under Mitsunobu conditions gave piperazine **13** exclusively by ^{1}H NMR in 71% isolated yield (entry 1). Addition of stoichiometric $Et_3N{\cdot}HCl$ to pure **12** (entry 3) was found to completely reverse the mode of cyclisation and give aziridine **14** exclusively by ^{1}H NMR in 83% isolated yield. A catalytic quantity of $Et_3N{\cdot}HCl$ also perturbed the cyclisation mode (entry 4) to a 3 : 7 mixture of **13** : **14**, highlighting that even a small impurity from tosylation can have a dramatic effect on the Mitsunobu cyclisation. Changing the solvent from THF to CH_2Cl_2 reduced the selectivity of the Mitsunobu cyclisation and led to a lower yield of isolated products (entry 2). The effect of adventitious water in the reaction was also considered and addition of a stoichiometric amount favoured aziridine **14**, but in only 50% conversion (entry 5) and proved anhydrous reaction conditions were necessary for full conversion. Both products (**13**, **14**) and the byproduct from DEAD, diethyl hydrazidodicarboxylate, were added in sub-stoichiometric (0.1 eq.) quantities and in all cases had no effect on the course of the reaction (entries 6–8). These experiments show that for these types of ambidentate substrates standard Mitsunobu cyclisation favours 6-*exo*-tet cyclisation by the tosyl protected amine, while addition of $Et_3N{\cdot}HCl$ favours 3-*exo*-tet cyclisation by the more electron rich secondary amine.

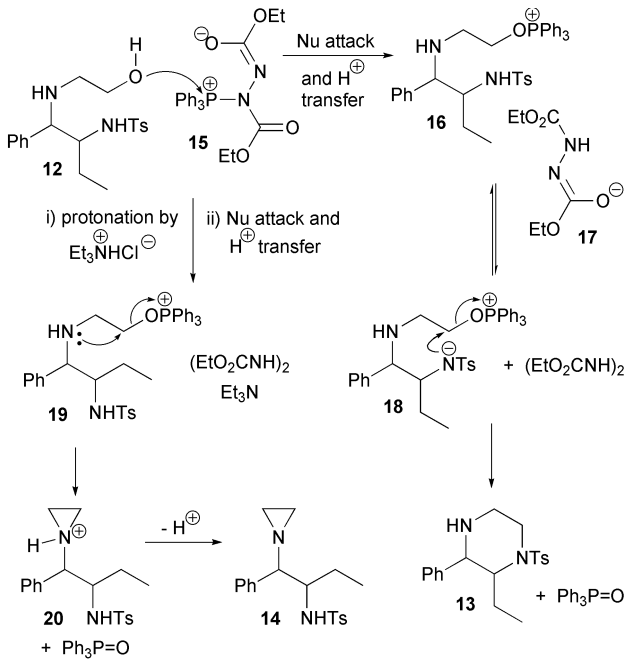
We postulate that the regiochemical switching of the Mitsunobu cyclisation can be explained by considering the accepted mechanism of the Mitsunobu reaction.[17b,20] In the absence of $Et_3N{\cdot}HCl$,

Table 1 Effect of additives on the mode of Mitsunobu cyclisation of **12**[a]

Entry	Additive	Mol% additive	Solvent	Conversion (%)	Ratio[b] **13** : **14**
1	None	—	THF	>95%[c]	>95 : 5
2	None	—	CH_2Cl_2	>95%	85 : 15
3	$Et_3N{\cdot}HCl$	1.0	THF	>95%[d]	<5 : 95
4	$Et_3N{\cdot}HCl$	0.2	THF	>95%	30 : 70
5	H_2O	1.0	THF	50%	<5 : 95
6	**13**	0.1	THF	>95%	>95 : 5
7	**14**	0.1	THF	>95%	>95 : 5
8	$(EtO_2CNH)_2$[e]	0.1	THF	>95%	>95 : 5

[a] **12** (1 eq.), solvent (2.5 mL), PPh_3 (1.4 eq.), DEAD (1.4 eq.), rt, 16 h. [b] Calculated from ^{1}H NMR spectra. [c] 71% isolated yield. [d] 83% isolated yield. [e] Diethyl hydrazidodicarboxylate.

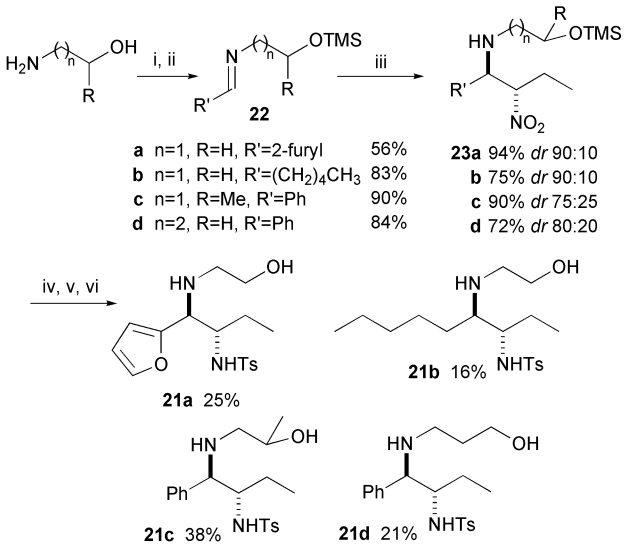
the primary alcohol of **12** attacks the phosphonium centre of betaine[21] **15** with concomitant proton transfer to give activated alcohol **16** and **17** (Scheme 3). Deprotonation of NHTs in **16** [pK_a(DMSO) ~16][22] by **17** [pK_a(DMSO) ~20][23] generates an aza nucleophile **18** in preparation for 6-*exo*-tet cyclisation to give piperazine **13**. In the presence of $Et_3N{\cdot}HCl$ [pK_a(DMSO) 9.0][24] we suggest this weak acid at some point protonates the carbamate function in **15**, the primary alcohol of **12** attacks the phosphonium centre, with concomitant proton transfer as before, to give activated alcohol **19**, diethyl hydrazidodicarboxylate $(EtO_2CNH)_2$ and Et_3N. Cyclisation of the more nucleophilic secondary amine of **19** in a 3-*exo*-tet manner gives protonated aziridine **20** [pK_a(DMSO) <10],[25] which provides an acidic proton to intercept **15** as $Et_3N{\cdot}HCl$ did (Scheme 3).



Scheme 3 Suggested mechanistic explanation for regiochemical switching of Mitsunobu cyclisation.

With procedures for the regiochemical switching of Mitsunobu cyclisation of the 1,2-diamine **12** determined, substrates **21a–d** were chosen to investigate the wider scope of this method. Substrates **21a** and **21b** containing an identical 2-aminoethanol appendage would probe the generality of the cyclisation with respect to other 1,2-diamines we can synthesise. Substrate **21c** would probe whether the 3-*exo*-tet cyclisation path to aziridines was possible at an activated secondary carbon and substrate **23d** would probe whether the formation of an azetidine was possible. The syntheses of diastereomerically pure materials were accomplished by the same route as for the preparation of **12** (Scheme 4). Stereochemistry was inferred by analogy to previous examples that have been correlated by single X-ray crystallography.[2,4,5]

Substrates **21a–d** containing the required hydroxyl and *N*-Ts functionality were screened under Mitsunobu cyclisation conditions with and without $Et_3N{\cdot}HCl$ [eqn (2) and Table 2]. Under the standard conditions the 2-aminoethanol derived substrates **21a** and **21b** gave complete conversion to the cyclised products **24/25a** and **24/25b** in 67% and 75% yield respectively (Table 2, entries 1 and 3). The ratio of the piperazine **24a**,**b** to aziridine **25a**,**b** was lower than with substrate **12** (65 : 35, 80 : 20 *versus* 95 : 5 respectively). Addition of $Et_3N{\cdot}HCl$ to the Mitsunobu cyclisation of **21a** successfully reversed the regioselectivity to give a preponderance of aziridine **25a** (entry 2, 35 : 65). Unfortunately addition of either stoichiometric or catalytic quantities of $Et_3N{\cdot}HCl$ to the cyclisation of **21b** seemed to impede cyclisation, only giving trace conversion to the expected aziridine **25b** in 10% yield (entries 4 and 5) with 40% recovered starting material and evidence of degradation. The failure of this substrate toward aziridine formation remains a mystery, but highlights that $Et_3N{\cdot}HCl$ inhibits cyclisation from the tosyl amine. Cyclisation of **21c** containing a secondary hydroxyl group gave a low yield of aziridne **25c** with both protocols (48% and with $Et_3N{\cdot}HCl$ 34%, entries 6 and 7). This highlights that the secondary centre decreases the yield of cyclisation and that the 6-*exo*-tet cyclisation mode is more sensitive toward steric hindrance. Cyclisation of **21d** under the standard conditions successfully gave 1,4-diazepane **24d** in 71% yield (entry 8). Addition of $Et_3N{\cdot}HCl$ however gave substitution



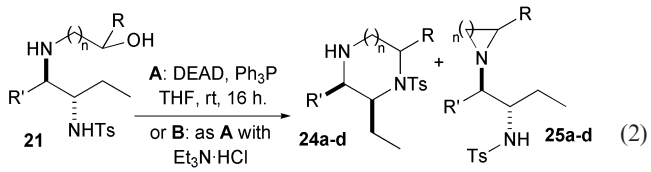
Scheme 4 *Reagents and conditions*: i, TMSCl, DMAP, Et_3N, CH_2Cl_2, −15 °C then rt, 16 h, ii, PhCHO, CH_2Cl_2, 4 Å MS, rt, 16 h, iii, 1-nitropropane, *n*-BuLi, THF, −78 °C, 10 min, AcOH, −78 °C then rt, 30 min, iv, Al–Hg, MeOH, THF, 5 °C then rt, v, $LiAlH_4$, Et_2O, 0 °C then rt, 16 h, vi, TsCl, Et_3N, THF, rt, 16 h.

Table 2 Scope of the Mitsunobu cyclisation of 1,2-diamines[a]

Entry	Substrate	Mitsunobu protocol	Isolated yield (%)	Ratio[c] **24** : **25**
1	**21a**	A	67	65 : 35
2	**21a**	B	76	35 : 65
3	**21b**	A	75	80 : 20
4	**21b**	B	~10[c]	0 : 100
5	**21b**	B[b]	~10[c]	0 : 100
6	**21c**	A	48	5 : 95
7	**21c**	B	34	0 : 100
8	**21d**	A	71	95 : 5
9	**21d**	B	92	—[d]

[a] **21** (1 eq.), solvent (2.5 mL), PPh_3 (1.4 eq.), DEAD (1.4 eq.), rt, 16 h. [b] 0.2 eq. $Et_3N{\cdot}HCl$. [c] Calculated from ^1H NMR spectra. [d] Complete conversion to chloride of **21d**.

of the hydroxyl group for chlorine in 92% yield (entry 9). This reflects the higher activation barrier associated with synthesising 4-membered rings and again the inhibiting effect of $Et_3N{\cdot}HCl$.



(2)

a n=1, R=H, R'=2-furyl
b n=1, R=H, R'=$(CH_2)_4CH_3$
c n=1, R=Me, R'=Ph
d n=2, R=H, R'=Ph

Conclusion

This research has demonstrated that the Mitsunobu reaction can be used to cyclise ambident 1,2-diamine systems *via* nucleophilic substitution at a carbon centre bearing a primary hydroxyl functionality. The regiochemistry of the Mitsunobu reaction, with respect to either the tosyl amide or secondary amino function, could be altered by the addition of $Et_3N{\cdot}HCl$. This additive was postulated to deter tosyl amide deprotonation and encourage cyclisation by the secondary amine to give aziridine products. In some substrates addition of $Et_3N{\cdot}HCl$ to the Mitsunobu reaction appeared to have a detrimental effect on the reaction, either leading to a lower isolated yield of the aziridine ring systems or shutting the reaction down completely. Alternatively this could reflect the difficulty in forming three membered rings with respect to six membered rings. Piperazine, 1,4-diazepane and aziridine ring systems, that are all structural motifs in nature, were successfully synthesised. The difficulty associated with the synthesis of piperazines by nucleophilic attack at a more functionalised carbon centre and the formation of azetidine ring systems highlights the inherent susceptibility of the Mitsunobu cyclisation approach to steric and ring strain factors and thereby limits the scope of the methodology. Despite the regiochemical problems faced in this work by the ambident nature of the nucleophilic 1,2-diamines the synthesis of a variety of cyclic systems has successfully demonstrated the potential of the nitro-Mannich reaction in synthesis.

Experimental

Our general experimental details have been published previously.[3,4] ^1H and ^{13}C NMR spectra were recorded as dilute solutions in C_6D_6 and IR were recorded as a thin film unless otherwise stated.

Benzylidene-(2-trimethylsilanyloxy-ethyl)-amine (10)

To a solution of 2-ethanolamine (1.80 mL, 29.1 mmol) in CH_2Cl_2 (60 mL) was added Et_3N (4.87 mL, 34.9 mmol, 1.2 eq.) and DMAP (36 mg, 1 mol%). The reaction was cooled to −15 °C and stirred for 10 min before the addition of TMSCl (4.85 mL, 38.4 mmol, 1.3 eq.), to give a cloudy solution that was allowed to warm to rt and left to stir for 16 h. The reaction was washed with water (30 mL), dried ($MgSO_4$), filtered through celite® and concentrated *in vacuo* to give crude 2-trimethylsilanyloxy-ethylamine as a yellow liquid (3.40 g, 25.5 mmol, 88%), in >95% purity by ^1H NMR, IR ν_{max}/cm^{-1} 3363 (N–H), 3500 (N–H), 2956–2600 (C–H), 1604 (N–H), 1251 (Si–C); δ_H ($CDCl_3$) 0.12 (9H, s, SiMe_3), 0.87 (2H, b, NH_2), 2.79 (2H, t, *J* 5.3, CH_2N), 3.60 (2H, t, *J* 5.3, CH_2O); δ_C ($CDCl_3$) 0.0 (CH_3), 44.6 (CH_2), 65.0 (CH_2); *m/z* 134.0996 (MH^+, 100%, $C_5H_{15}NOSi$ requires 134.1002).

To a solution of crude 2-trimethylsilanyloxy-ethylamine formed as above (6.69 g, 50.2 mmol) in CH_2Cl_2 (250 ml) was added rigorously dried 4 Å molecular sieves (5.00 g). The suspension was stirred at rt for 5 min and benzaldehyde (5.60 mL, 55.1 mmol, 1.1 eq.) added. The mixture was left to stir at rt for 16 h, filtered through celite® and the solvent evaporated *in vacuo* to yield the crude imine as a yellow liquid (9.02 g, 40.8 mmol, 81%) in >95% purity by ^1H NMR that was unstable at rt, IR ν_{max}/cm^{-1} 3500–3282 (N–H), 3062–2868 (C-H), 1648 (C=N), 1251 (Si–C), 841 (Si–C); δ_H 0.12 (9H, s, SiMe_3), 3.67 (2H, td, *J* 5.7, 1.2, CH_2N), 3.88 (2H, t, *J* 5.7, CH_2O), 7.09–7.17 (3H, m, Ar*H*), 7.76–7.78 (2H, m, Ar*H*), 8.05 (1H, bs, C*H*=N); δ_C 0.0 (CH_3), 62.9 (CH_2), 64.3 (CH_2), 128.7 (CH), 128.9 (CH), 130.8 (CH), 137.3 (C_q), 162.1 (CH); *m/z* (EI^+) 222.1305 (MH^+, 100%, $C_{12}H_{20}NOSi$ requires 222.1309), 150 (7).

(2-Nitro-1-phenyl-butyl)-(2-trimethylsilanyloxy-ethyl)-amine (11)

To a solution of 1-nitropropane (0.13 ml, 1.40 mmol. 1.4 eq.) in THF (20 ml) at −78 °C was added dropwise *n*-BuLi (2.5 M in hexane, 0.56 ml, 1.4 mmol, 1.4 eq.) and the solution stirred for a further 10 min. A solution of crude imine **10** (0.221 g, 1.00 mmol) in THF (10 mL) was added *via* cannula, the mixture stirred for 10 min and AcOH (0.14 mL, 2.4 mmol, 2.4 eq.) added dropwise. The reaction was stirred for 20 min at −78 °C and then warmed to rt for a further 30 min. The reaction was quenched by addition of sat. $NaHCO_3$ (10 mL) and extracted into Et_2O (20 mL). The organic phase was washed with $NaHCO_3$ (10 mL), dried ($MgSO_4$) and concentrated *in vacuo* to yield the crude β-nitroamine **11** (223 mg, 0.720 mmol, 72%, de >95%) as a cloudy oil in >95% purity by ^1H NMR, IR ν_{max}/cm^{-1} 3338 (N–H), 3064–2880 (C–H), 1551 (N–O), 1375 (N–O), 1251 (Si–C), 1093 (C–N), 843 (Si–C); δ_H 0.08 (9H, s, SiMe_3), 0.64 (3H, t, *J* 7.3, CH_2CH_3), 1.70 (1H, dqd, *J* 14.8, 7.5, 2.9, C$H_2$$CH_3$), 1.97 (1H, ddq, *J* 14.5, 11.0, 7.2, C$H_2$$CH_3$), 2.34 (1H, ddd, *J* 11.7, 6.2, 3.7, CH_2N), 2.41 (1H, ddd, *J* 11.9, 6.2, 3.9, CH_2N), 3.38–3.48 (2H, m, CH_2O), 3.97 (1H, d, *J* 6.4, C*H*Ph), 4.33–4.39 (1H, m, C*H*NO_2), 7.02–7.14 (5H, m, Ar*H*); δ_C −0.7 (CH_3), 10.0 (CH_3), 22.6 (CH_2), 49.4 (CH_2), 61.6 (CH_2), 65.1 (CH), 94.8 (CH), 127.1 (CH), 128.1 (CH), 128.6 (CH), 139.1 (C_q); *m/z* (EI^+) 311.1785 (MH^+, 100%, $C_{15}H_{27}N_2O_3Si$ requires 311.1785), 222 (78); Diastereoselectivity calculated by analysis of the ^1H NMR integrals for the CH_2CH_3 protons, 0.55^{syn}, 0.64^{anti}.

2-(2-Amino-1-phenyl-butylamino)-ethanol (9)

To a stirred solution of crude β-nitroamine **11** (2.60 g, 8.38 mmol) in THF (84 mL) at 5 °C was added portionwise MeOH (3.39 mL, 83.8 mmol, 10 eq.) and freshly amalgamated Al foil (746 mg, 27.7 mmol, 3.3 eq.). [Coils of Al foil (~1 mmol) were soaked in ether to remove machining oils and individually amalgamated by immersion in a stirring sat. $HgCl_{2(aq)}$ solution (30 s), washed by immersion in H_2O (5 s) then ether (5 s), roughly dried on tissue and added to the reaction mixture.] The reaction mixture was allowed to warm to 25 °C and stirred for 1 h to give a grey suspension. The reaction mixture was filtered through celite®, washed with THF (2 × 40 mL), MeOH (40 mL) and evaporated

in vacuo. The product was dissolved in Et_2O (80 mL), washed with water (40 mL), dried ($MgSO_4$), filtered and evaporated to leave the crude monoprotected hydroxylamine (2.21 g, 7.47 mmol, 89%) as a cloudy liquid which was reduced further without purification.

Data for *N*-{1-[phenyl-(2-trimethylsilanyloxy-ethylamino)-methyl]-propyl}-hydroxylamine; IR ν_{max}/cm^{-1} 3350–3100 (N–H, O–H), 3062–2873 (C–H), 1251 (Si–C), 842 (Si–C); δ_H 0.10 (9H, s, Si*Me*$_3$), 0.77 (3H, t, *J* 7.5, CH_2CH_3), 1.24-1.35 (1H, m, CH_2CH_3), 1.41 (1H, dqd, *J* 14.2, 7.6, 4.1, CH_2CH_3), 2.56 (1H, ddd, *J* 12.2, 5.7, 4.0, CH_2N), 2.70 (1H, ddd, *J* 12.2, 7.2, 4.1, CH_2N), 3.07 (1H, dt, *J* 9.0, 3.9, C*H*NOH), 3.45 (1H, ddd, *J* 10.3, 5.7, 4.1, CH_2O), 3.62 (1H, ddd, *J* 10.3, 7.2, 3.8, CH_2O), 4.23 (1H, d, *J* 4.0, C*H*N), 7.10 (1H, t, *J* 7.3, Ar*H*), 7.22 (2H, t, *J* 7.6, Ar*H*), 7.42 (2H, t, *J* 7.4, Ar*H*); δ_C −0.5 (CH_3), 11.4 (CH_3), 19.8 (CH_2), 49.7 (CH_2), 61.8 (CH_2), 65.3 (CH), 68.4 (CH), 127.0 (CH), 128.1 (CH), 128.4 (CH), 141.6 (C_q); *m*/*z* (EI$^+$) 297.1981 (MH^+, 100%, $C_{15}H_{29}N_2O_2Si$ requires 297.1993), 224 (17).

To a stirred solution of $LiAlH_4$ (176 mg, 4.64 mmol, 2 eq.) in dry Et_2O (80 mL) at 0 °C was added dropwise the crude hydroxylamine from above (2.21 g, 7.47 mmol) in dry Et_2O (17 mL) and warmed to rt for 16 h. The resulting grey suspension was cooled to 0 °C and quenched by dropwise addition of ^{i}PrOH (1.62 mL) and brine (0.46 mL). The reaction was dried ($MgSO_4$), filtered through celite® and evaporated to yield the crude diamine **9** (1.19 g, 5.74 mmol, 71% over 2 steps); IR ν_{max}/cm^{-1} 3350–3100 (N–H/O–H), 3061–2850 (C–H), 1602 (N–H), 1126 (C–N); δ_H 0.97 (3H, t, *J* 7.4, CH_2CH_3), 1.08-1.16 (1H, m, CH_2CH_3), 1.28 (1H, d, *J* 6.1, N*H*), 1.50-1.61 (1H, dqd, *J* 13.7, 7.5, 4.1, CH_2CH_3), 2.10 (1H, b, O*H*), 2.60 (1H, ddd, *J* 12.4, 6.1, 3.9, CH_2N), 2.66 (1H, ddd, *J* 12.4, 6.7, 4.0, CH_2N), 2.88 (1H, ddd, *J* 9.1, 4.6, 3.3, C*H*NH$_2$), 3.57 (1H, ddd, *J* 11.0, 6.1, 4.0, CH_2O), 3.61 (1H, d, *J* 4.7, C*H*N), 3.63–3.69 (1H, m, CH_2O), 7.26–7.39 (5H, m, Ar*H*); δ_C 10.9 (CH_3), 27.3 (CH_2), 49.0 (CH_2), 57.4 (CH), 61.3 (CH_2), 67.1 (CH), 127.3 (CH), 128.2 (CH), 128.3 (CH), 128.5 (CH), 140.4 (C_q); *m*/*z* (EI$^+$) 209.1646 (MH^+, 7%, $C_{12}H_{21}N_2O$ requires 209.1648), 192 (19), 148 (100).

N-{1-[(2-Hydroxy-ethylamino)-phenyl-methyl]-propyl}-4-methyl-benzenesulfonamide (12)

To a stirred solution of crude diamine **9** (480 mg, 2.32 mmol) in THF (23 mL) was added Et_3N (647 µL 4.64 mmol, 2.0 eq.) and TsCl (442 mg, 2.32 mmol, 1.0 eq.) and the reaction left to stir at rt for 16 h. The reaction was diluted with Et_2O (11 mL), washed with $NaHCO_3$ (11 mL) and the aqueous layer extracted into Et_2O (2 × 20 mL). The combined organic layers were washed with 1 M $NaOH_{(aq)}$ (11 mL), brine (11 mL), dried ($MgSO_4$) and evaporated *in vacuo* to leave the crude tosyl protected diamine. Purification by flash chromatography (R_f = 0.11, 1 : 2 hexanes : EtOAc) gave **12** (628 mg, 1.74 mmol, 75%) as a yellow solid, mp = 92–94 °C; IR (solution) ν_{max}/cm^{-1} 3696–3377 (O–H/N–H), 2937–2879 (C–H), 1341 (S=O), 1155 (S=O), 1092 (C–N); δ_H 0.73 (3H, t, *J* 7.3, CH_2CH_3), 1.08–1.33 (2H, m, CH_2CH_3), 2.41–2.47 (1H, m, CH_2N), 2.46 (3H, s, ArCH_3), 2.67 (1H, ddd, *J* 12.4, 7.4, 3.8, CH_2N), 3.40 (1H, b, C*H*NHTs), 3.47–3.63 (2H, m, CH_2O), 3.66 (1H, d, *J* 3.4, PhC*H*), 7.14 (2H, bd, *J* 7.0, Ar*H*), 7.25–7.38 (5H, m, Ar*H*), 7.83 (2H, d, *J* 8.2, Ar*H*); δ_C 10.8 (CH_3), 21.6 (CH_3), 22.6 (CH_2), 49.2 (CH_2), 60.4 (CH), 61.3 (CH_2), 64.5 (CH), 127.2 (CH), 127.5 (CH), 128.6 (CH), 129.7 (CH), 138.3 (C_q), 139.3 (C_q), 143.4 (C_q); *m*/*z* 363.1731 (MH^+, 100%, $C_{19}H_{27}N_2O_3S$ requires 363.1748).

2-Ethyl-3-phenyl-1-(toluene-4-sulfonyl)-piperazine (13)

To a stirred solution of diamine **12** (202 mg, 0.569 mmol) in THF (20 mL) was added PPh_3 (209 mg, 0.797 mmol, 1.4 eq.). The mixture was stirred at rt for 10 min before addition of DEAD (126 µL, 0.797 mmol, 1.4 eq.) and the reaction left to stir at rt for 16 h. The reaction was concentrated *in vacuo* to leave the crude product. Purification by flash chromatography (R_f = 0.43, 1 : 2 hexanes : EtOAc) gave **13** (140 mg, 0.403 mmol, 71%) as a pale cream solid, mp 111–112 °C; IR ν_{max}/cm^{-1} 3320–3200 (N–H), 2965–2875 (C–H), 1341 (S=O), 1158 (S=O), 1095 (C–N); δ_H ($CDCl_3$) 0.66 (3H, t, *J* 7.4, CH_2CH_3), 1.08 (1H, dqd, *J* 14.5, 7.3, 4.3, CH_2CH_3), 1.69–1.82 (2H, m, CH_2CH_3/N*H*), 2.45 (3H, s, ArCH_3), 2.75 (1H, td, *J* 12.1, 3.4, CH_2N), 2.93–2.98 (1H, m, CH_2N), 3.15–3.24 (1H, m, CH_2N), 3.77–3.84 (2H, m, CH_2N/C*H*Ph), 3.96 (1H, dt, *J* 10.4, 3.9, C*H*NTs), 7.24–7.38 (7H, m, Ar*H*), 7.72–7.76 (2H, d, *J* 8.2, Ar*H*); δ_C ($CDCl_3$) 10.7 (CH_3), 16.6 (CH_2), 21.6 (CH_3), 40.5 (CH_2), 45.9 (CH_2), 60.3 (CH), 62.1 (CH), 126.6 (CH), 127.2 (CH), 127.4 (CH), 128.5 (CH), 129.8 (CH), 139.2 (C_q), 140.9 (C_q), 143.1 (C_q); *m*/*z* 345.1630 (MH^+, 100%, $C_{19}H_{25}N_2O_2S$ requires 345.1631).

N-[1-(Aziridin-1-yl-phenyl-methyl)-propyl]-4-methyl-benzenesulfonamide (14)

To a stirred solution of diamine **12** (54 mg, 0.15 mmol) in THF (20 mL) was added $Et_3N{\cdot}HCl$ (21 mg, 0.15 mmol, 1.0 eq.). The mixture was stirred for 10 min before addition of PPh_3 (55 mg, 0.21 mmol, 1.4 eq.) and DEAD (33 µL, 0.21 mmol, 1.4 eq.) and the reaction left to stir at rt for 16 h. The reaction was concentrated *in vacuo* to leave the crude product. Purification by flash chromatography (R_f = 0.32, 1 : 2 hexanes : EtOAc) gave **14** (43 mg, 0.12 mmol, 83%) as a pale cream solid mp 89–90 °C; IR ν_{max}/cm^{-1} 3293 (N–H), 3062–2876 (C–H), 1320 (S=O), 1161 (S=O), 1093 (C–N); δ_H ($CDCl_3$) 0.61 (3H, t, *J* 7.4, CH_2CH_3), 0.91 (1H, dd, *J* 7.1, 4.2, CH_2N), 1.36–1.55 (2H, m, CH_2CH_3), 1.45 (1H, dd, *J* 7.1, 4.0, CH_2N), 1.62 (1H, dd, *J* 5.8, 4.0, CH_2N), 1.78 (1H, dd, *J* 5.9, 4.2, CH_2N), 2.39 (3H, s, ArCH_3), 2.60 (1H, d, *J* 3.3, C*H*Ph), 3.29–3.35 (1H, m, C*H*NTs), 4.60 (1H, d, *J* 7.2, N*H*), 7.20–7.30 (7H, m, Ar*H*), 7.72–7.76 (2H, dt, *J* 8.3, 1.8, Ar*H*); δ_C ($CDCl_3$) 10.6 (CH_3), 21.6 (CH_3), 23.0 (CH_2), 25.9 (CH_2), 29.8 (CH_2), 61.1 (CH), 76.3 (CH), 127.3 (CH), 127.4 (CH), 128.3 (CH), 129.5 (CH), 138.0 (C_q), 139.9 (C_q), 143.2 (C_q); *m*/*z* 345.1639 (MH^+, 100%, $C_{19}H_{25}N_2O_2S$ requires 345.1637).

Furan-2-ylmethylene-(3-trimethylsilanyloxy-ethyl)-amine (22a)

Synthesised in a similar manner to that described for **10**. Crude 2-trimethylsilanyloxy-ethylamine (3.37 g, 25.0 mmol) and 2-furanaldehyde (2.40 g, 25.0 mmol) gave crude **22a** (3.39 g, 16.1 mmol, 64%) as a yellow oil in >95% purity by ^{1}H NMR, IR ν_{max}/cm^{-1} 2956–2800 (C–H), 1645 (C=N), 1251 (Si–C), 841 (Si–C); δ_H 0.09 (9H, s, Si*Me*$_3$), 3.57 (1H, d, *J* 6.2, 0.9, CH_2N), 3.81 (2H, t, *J* 5.7, CH_2O), 5.99 (1H, dd, *J* 3.4, 1.8, Fur*H*), 7.28 (1H, d, *J* 3.4, Fur*H*), 7.61 (1H, d, *J* 1.5, Fur*H*), 7.92 (1H, bs, C*H* = N); δ_C 0.0 (CH_3), 62.8 (CH_2), 64.4 (CH_2), 111.9 (CH), 112.3 (CH),

128.5 (CH), 144.4 (C_q), 151.3 (CH); *m/z* 212.1107 (MH^+, 100%, $C_{10}H_{19}NO_2Si$ requires 212.1104).

Hexylidene-(2-trimethylsilanyloxy-ethyl)-amine (22b)

Synthesised in a similar manner to that described for **10** except pre-cooled hexanal (2.58 mL, 21.5 mmol) was added to a solution of crude 2-trimethylsilanyloxy-ethylamine (2.87 g, 21.5 mmol) in CH_2Cl_2 at. −78 °C, the reaction was stirred at −78 °C for 30 min, filtered and evaporated to give **22b** (4.35 g, 20.2 mmol, 94%) as a yellow oil in >95% purity by ^{1}H NMR that was used immediately, IR ν_{max}/cm^{-1} 2956–2860 (C–H), 1672 (C=N), 1251 (Si–C), 842 (Si–C); δ_H 0.09 (9H, s, Si*Me*$_3$), 0.84 (3H, t, *J* 6.8, C*H*$_3$), 1.13–1.29 (4H, m, C*H*$_2$), 1.43 (2H, p, *J* 7.2, C*H*$_2$), 2.09–2.14 (2H, m, C*H*$_2$), 3.44 (2H, t, *J* 5.5, C*H*$_2$N), 3.76 (2H, t, *J* 5.7, C*H*$_2$O), 7.41 (1H, s, C*H*N); δ_C −0.1 (CH_3), 14.3 (CH_3), 23.0 (CH_2), 26.0 (CH_2), 31.9 (CH_2), 36.1 (CH_2), 62.6 (CH_2), 63.9 (CH_2), 165.9 (CH). Compound **22b** was unstable to MS analysis.

Benzylidene-(2-trimethylsilanyloxy-propyl)-amine (22c)

Synthesised in a similar manner to that described for **10**, 3-amino-2-propanol (1.54 mL, 20.0 mmol) and TMSCl (2.70 mL, 21.1 mmol) gave crude 2-trimethylsilanyloxy-propylamine as a yellow liquid (2.29 g, 15.5 mmol, 78%) in >95% purity by ^{1}H NMR, δ_H ($CDCl_3$) 0.11 (9H, s, Si*Me*$_3$), 1.10 (3H, dd, *J* 6.2, 1.2, CHC*H*$_3$), 1.66 (2H, b, N*H*), 2.56 (1H, ddd, *J* 12.8, 7.1, 1.3, C*H*$_2$N), 2.62 (1H, ddd, *J* 12.9, 3.9, 1.1, C*H*$_2$N), 3.70–3.77 (1H, m, C*H*OTMS); δ_C ($CDCl_3$) 0.3 (CH_3), 21.2 (CH_3), 49.7 (CH_2), 70.1 (CH); *m/z* 148.1167 (MH^+, 100%, $C_6H_{18}NOSi$ requires 148.1152).

Crude 2-trimethylsilanyloxy-propylamine (2.20 g, 14.9 mmol) formed above and benzaldehyde (1.65 mL, 16.2 mmol) gave crude **22c** as a yellow liquid (3.33 g, 14.2 mmol, 95%) as a 10 : 1 mixture of OTMS and OH product that was unstable at room temperature, IR ν_{max}/cm^{-1} 3063–2841 (C–H), 1647 (C=N), 1250 (Si–C), 840 (Si–C); δ_H 0.12 (9H, s, Si*Me*$_3$), 1.24 (3H, d, *J* 6.2, CHC*H*$_3$), 3.51 (1H, bdd, *J* 11.4, 7.1, C*H*$_2$N), 3.64 (1H, ddd, *J* 11.4, 4.8, 1.3, C*H*$_2$N), 4.17–4.23 (1H, m, C*H*O), 7.10–7.18 (3H, m, Ar*H*), 7.77 (2H, d, *J* 7.0, Ar*H*), 8.03 (1H, bs, C*H*=N); δ_C 0.2 (CH_3), 22.3 (CH_3), 68.3 (CH), 69.6 (CH_2), 128.1 (CH), 128.2 (CH), 128.5 (CH), 136.9 (C_q), 161.6 (CH); *m/z* 236.1461 (MH^+, 100%, $C_{13}H_{22}NOSi$ requires 236.1465).

Benzylidene-(3-trimethylsilanyloxy-propyl)-amine (22d)

Synthesised in a similar manner to that described for **10**. 3-Amino-1-propanol (1.53 mL, 20.0 mmol) and TMSCl (3.22 mL 25.4 mmol) gave crude 3-trimethylsilanyloxy-propylamine (2.63 g, 17.7 mmol, 89%) as a yellow liquid in >95% purity by ^{1}H NMR, IR ν_{max}/cm^{-1} 3400–3200 (N–H), 2955–2850 (C–H), 1251 (Si–C), 839 (Si–C); δ_H ($CDCl_3$) 0.11 (9H, s, Si*Me*$_3$), 1.76 (2H, tt, *J* 6.8, 6.2, C*H*$_2$CH$_2$O), 1.71 (2H, b, N*H*$_2$), 2.79 (2H, t, *J* 6.8, C*H*$_2$N), 3.60 (2H, t, *J* 6.2, C*H*$_2$O); δ_C ($CDCl_3$) −0.5 (CH_3), 36.2 (CH_2), 39.4 (CH_2), 60.6 (CH_2); *m/z* 148.1155 (MH^+, 100%, $C_5H_{15}NOSi$ requires 148.1163).

Crude 3-trimethylsilanyloxy-propylamine (2.63 g, 17.7 mmol) formed from above and benzaldehyde (2.00 mL, 19.7 mmol) gave imine **22d** (3.62 g, 15.4 mmol, 86%) as a yellow liquid in >95% purity by ^{1}H NMR, that was unstable at rt, IR ν_{max}/cm^{-1} 3500–3250 (N–H), 3084–2738 (C–H), 1646 (C=N), 1251 (Si–C), 841 (Si–C); δ_H 0.13 (9H, s, Si*Me*$_3$), 1.98 (2H, p, *J* 6.2, C*H*$_2$CH$_2$), 3.65–3.70 (4H, m, C*H*$_2$N/C*H*$_2$O), 7.10–7.16 (3H, m, Ar*H*), 7.72–7.75 (1H, m, Ar*H*), 7.76–7.79 (1H, m, Ar*H*), 8.06 (1H, s, C*H*=N); δ_C −0.6 (CH_3), 34.1 (CH_2), 57.9 (CH_2), 59.9 (CH_2), 127.7 (CH), 127.9 (CH), 128.1 (CH), 130.3 (C_q), 160.5 (CH); *m/z* 236.1466 (MH^+, 100%, $C_{13}H_{22}NOSi$ requires 236.1465).

(1-Furan-2-yl-2-nitro-butyl)-(2-trimethylsilanyloxy-ethyl)-amine (23a)

Synthesised in a similar manner to that described for **11**. Crude imine **22a** (3.39 g, 16.1 mmol) gave crude β-nitroamine **23a** (4.53 g, 15.1 mmol, 94%, dr 90 : 10) as a yellow oil in >95% purity by ^{1}H NMR, IR ν_{max}/cm^{-1} 3400–3342 (N–H), 2957–2800 (C–H), 1552 (N–O), 1373 (N–O), 1095 (C–N); δ_H 0.05 (9H, s, Si*Me*$_3$), 0.69 (3H, t, *J* 7.4, CH$_2$C*H*$_3$), 1.76 (1H, b, N*H*), 1.82–1.98 (2H, m, C*H*$_2$CH$_3$), 2.32–2.40 (1H, m, C*H*$_2$N), 2.48–2.55 (1H, m, C*H*$_2$N), 3.38 (1H, ddd, *J* 10.2, 5.4, 4.2, C*H*$_2$O), 3.45 (1H, ddd, *J* 10.2, 7.5, 4.0, C*H*$_2$O), 4.09 (1H, bt, *J* 7.5, C*H*NH), 4.48 (1H, ddd, *J* 10.0, 7.6, 3.7 C*H*NO$_2$), 5.98 (1H, dd, *J* 3.2, 0.9, Fur*H*), 6.06 (1H, d, *J* 3.2, Fur*H*), 6.99 (1H, dd, *J* 1.8, 0.7, Fur*H*); δ_C −0.7 (CH_3), 10.1 (CH_3), 23.5 (CH_2), 49.7 (CH_2), 58.9 (CH), 61.9 (CH_2), 92.4 (CH), 108.4 (CH), 110.2 (CH), 128.1 (CH), 142.3 (CH), 152.3 (C_q); *m/z* 301.1584 (MH^+, 100%, $C_{13}H_{25}N_2O_4Si$ requires 301.1584). Diastereoselectivity calculated by analysis of the ^{1}H NMR integrals for the CH$_2$C*H*$_3$ protons, 0.60^{syn}, 0.69^{anti}.

[1-(1-Nitro-propyl)-hexyl]-(2-trimethylsilanyloxy-ethyl)-amine (23b)

Synthesised in a similar manner to that described for **11**. Crude imine **22b** (4.70 g, 21.8 mmol) gave crude β-nitroamine **23a** (5.00 g, 16.4 mmol, 75%, dr 90 : 10) as a yellow oil in >95% purity by ^{1}H NMR, IR ν_{max}/cm^{-1} 3364 (N–H), 2957–2861 (C–H), 1548 (N–O), 1377 (N–O), 1096 (C–N); δ_H 0.11 (9H, s, Si*Me*$_3$), 0.74 (3H, t, *J* 7.3, CH$_2$C*H*$_3$), 0.87 (3H, t, *J* 7.2, CH$_2$C*H*$_3$), 1.08–1.40 (8H, m, C*H*$_2$), 1.58 (1H, dqd, *J* 14.4, 7.2, 3.4, CHC*H*$_2$CH$_3$), 1.58 (1H, ddq, *J* 14.3, 10.7, 7.2, CHC*H*$_2$CH$_3$), 2.48–2.60 (2H, m, C*H*$_2$N), 2.77–2.82 (1H, m, C*H*NCH$_2$), 3.40–3.48 (2H, m, C*H*$_2$O), 4.23 (1H, ddd, *J* 10.5, 6.2, 3.2 C*H*NO$_2$); δ_C −0.7 (CH_3), 10.5 (CH_3), 14.0 (CH_3), 22.7 (CH_2), 23.0 (CH_2), 25.6 (CH_2), 31.1 (CH_2), 31.7 (CH_2), 49.6 (CH_2), 60.5 (CH), 62.2 (CH_2), 92.9 (CH); *m/z* 305.2237 (MH^+, 100%, $C_{14}H_{32}N_2O_3Si$ requires 305.2260). Diastereoselectivity calculated by analysis of the ^{1}H NMR integrals for the C*H*NO$_2$ protons, 4.23^{anti}, 4.40^{syn}.

(2-Nitro-1-phenyl-butyl)-(2-trimethylsilanyloxy-propyl)-amine (23c)

Synthesised in a similar manner to that described for **11**. Crude imine **22c** (2.35 g, 10.0 mmol) gave crude β-nitroamine **23c** (2.86 g, 8.80 mmol, 88%, dr 75 : 25) as a pale yellow oil in >95% purity by ^{1}H NMR, IR ν_{max}/cm^{-1} 3347 (N–H), 3100–2850 (C–H), 1551 (N–O), 1375 (N–O), 1251 (Si–C), 1094 (C–N), 842 (Si–C); δ_H 0.12 (9H, s, Si*Me*$_3$), 0.66 (3H, t, *J* 7.4, CH$_2$C*H*$_3$), 0.99 (3H, d, *J* 6.2, CHC*H*$_3$), 1.72 (1H, dqd, *J* 14.7, 7.3, 3.0, C*H*$_2$CH$_3$), 1.93–2.02 (1H, m, C*H*$_2$CH$_3$), 2.23 (1H, dd, *J* 11.6, 3.7, C*H*$_2$N), 2.34 (1H, dd, *J* 11.6, 7.1, C*H*$_2$N), 3.71–3.78 (1H, m, C*H*O), 4.03 (1H, d, *J* 6.1, C*H*Ph), 4.42 (1H, ddd, *J* 10.8, 6.3, 3.0, C*H*NO$_2$), 7.02–7.21 (5H, m, Ar*H*); δ_C 0.1 (CH_3), 10.3 (CH_3), 21.5 (CH_3), 22.5 (CH_2),

54.9 (CH_2), 65.1 (CH), 67.8 (CH), 94.8 (CH), 127.7 (CH), 127.9 (CH), 128.1 (CH), 139.1 (C_q); *m/z* (EI$^+$) 325.1934 (MH$^+$, 100%, $C_{16}H_{29}N_2O_3Si$ requires 325.1942) 236 (78). Diastereoselectivity calculated by analysis of the ^{1}H NMR integrals for the C*H*Ph protons, 3.95^{syn}, 4.03^{anti}.

(2-Nitro-1-phenyl-butyl)-(3-trimethylsilanyloxy-propyl)-amine (23d)

Synthesised in a similar manner to that described for **11**. Crude imine **22d** (3.60 g, 15.3 mmol) gave 85% conversion to crude β-nitroamine **23d** (4.22 g, 72% β-nitroamine, dr 80 : 20) as a yellow oil, IR ν_{max}/cm^{-1} 3500–3344 (O–H/N–H), 3064–2800 (C–H), 1551 (N–O), 1375 (N–O), 1251 (Si–C), 1093 (C–N), 841 (Si–C); δ_H 0.09 (9H, s, Si*Me*$_3$), 0.67 (3H, t, *J* 7.4, CH_2CH_3), 1.51 (2H, p, *J* 6.5, CH_2CH_2O), 1.68–1.78 (1H, m, CH_2CH_3), 1.90–2.01 (1H, m, CH_2CH_3), 2.32–2.39 (1H, m, CH_2N), 2.43–2.50 (1H, m, CH_2N), 3.46 (2H, t, *J* 6.0, CH_2O), 3.67 (1H, q, *J* 6.4, N*H*), 3.94 (1H, d, *J* 6.0, C*H*Ph), 4.34–4.39 (1H, m, C*H*NO_2), 7.01–7.15 (5H, m, Ar*H*); δ_C −0.7 (CH_3), 10.3 (CH_3), 22.9 (CH_2), 32.8 (CH_2), 45.1 (CH_2), 60.8 (CH_2), 65.4 (CH), 94.7 (CH), 127.7 (CH), 127.9 (CH), 128.1 (CH), 139.2 (C_q); *m/z* (EI$^+$) 325.1961 (MH$^+$, 100%, $C_{16}H_{29}N_2O_3Si$ requires 325.1942), 253 (27), 236 (42). Diastereoselectivity calculated by analysis of the ^{1}H NMR integrals for the C*H*Ph protons, 3.81^{syn}, 3.94^{anti}.

N-[1-Ethyl-2-(furany-2-yl)-2-(2-hydroxy-ethylamino)-ethyl]-4-methyl-benzenesulfonamide (21a)

Synthesised in a similar manner to first **9** then **11**. Treatment of β-nitroamine **23a** (1.55 g, 5.16 mmol) with Al–Hg amalgam gave *N*-{1-[furan-2-yl-(2-trimethylsilanyloxy-ethylamino)-methyl]-propyl}-hydroxylamine (1.40 g, 4.89 mmol, 95%) as a yellow oil that was unstable to chromatography, IR ν_{max}/cm^{-1} 3300–3100 (O–H/N–H), 2958–2875 (C–H), 1252 (Si–C), 1085 (C–N), 842 (Si–C); δ_H 0.09 (9H, s, Si*Me*$_3$), 0.88 (3H, t, *J* 7.5, CH_2CH_3), 1.28–1.38 (1H, m, CH_2CH_3), 1.46 (1H, dqd, *J* 14.0, 7.5, 4.3, CH_2CH_3), 2.57 (1H, ddd, *J* 11.9, 4.9, 4.0, CH_2N), 2.78 (1H, ddd, *J* 12.0, 7.9, 4.3, CH_2N), 3.22 (1H, dt, *J* 9.0, 4.1, C*H*NOH), 3.47–3.48 (1H, m, CH_2O), 3.56–3.61 (1H, m, CH_2O), 4.33 (1H, d, *J* 3.9, FurC*H*N), 6.11 (1H, dd, *J* 3.2, 1.8, Fur*H*), 6.20 (1H, dt, *J* 3.2, 0.7, Fur*H*), 7.09 (1H, dd, *J* 1.8, 0.8, Fur*H*); δ_C −0.6 (CH_3), 11.5 (CH_3), 20.5 (CH_2), 50.2 (CH_2), 57.0 (CH), 62.0 (CH_2), 66.9 (CH), 107.0 (CH), 110.2 (CH), 141.5 (CH), 155.8 (C_q); *m/z* 287.1778 (MH$^+$, 100%, $C_{13}H_{27}N_2O_3Si$ requires 287.1791).

Reduction of the hydroxylamine formed above with $LiAlH_4$ gave 1-furan-2-yl-*N*^{1}-(2-trimethylsilanyloxy-ethyl)-butane-1,2-diamine (978 mg, 3.62 mmol, 70%) as a yellow oil that was unstable to chromatography, IR ν_{max}/cm^{-1} 3500–3100 (O–H/N–H), 2959–2875 (C–H), 1598 (N–H), 1252 (Si–C), 843 (Si–C); δ_H 0.11 (9H, s, Si*Me*$_3$), 0.96 (3H, t, *J* 7.4, CH_2CH_3), 1.12–1.22 (1H, m, CH_2CH_3), 1.49 (1H, dqd, *J* 13.7, 7.5, 4.7, CH_2CH_3), 2.62 (1H, ddd, *J* 12.5, 6.3, 3.8, CH_2N), 2.72 (1H, ddd, *J* 12.5, 6.8, 3.8, CH_2N), 2.91 (1H, dt, *J* 8.5, 4.8, C*H*NH_2), 3.61–3.69 (3H, m, CH_2O, N*H*), 3.66 (1H, d, *J* 4.8, FurC*H*N), 6.21–6.22 (1H, m, Fur*H*), 6.34 (1H, dd, *J* 3.2, 0.8, Fur*H*), 7.38 (1H, dd, *J* 1.8, 0.8, Fur*H*); δ_C −0.4 (CH_3), 10.9 (CH_3), 28.0 (CH_2), 49.0 (CH_2), 56.3 (CH), 60.5 (CH), 61.1 (CH_2), 108.0 (CH), 110.0 (CH), 141.9 (CH), 154.4 (C_q); *m/z* 271.1828 (MH$^+$, 100%, $C_{13}H_{27}N_2O_2Si$ requires 271.1836).

Tosylation of the primary amine of the diamine formed above (970 mg, 3.60 mmol) gave crude **21a** (1.30 g, 3.06 mmol, 85%) as a brown oil. Purification by flash chromatography gave pure **21a** (438 mg, 1.24 mmol, 35%) as an orange oil, IR ν_{max}/cm^{-1} 3310 (N–H), 2965–2877 (C–H), 1598 (N–H), 1325 (S=O), 1160 (S=O), 1093 (C–N); δ_H 0.76 (3H, t, *J* 7.4, CH_2CH_3), 1.18–1.28 (2H, m, CH_2CH_3), 1.70 (1H, b, N*H*), 2.42 (3H, s, ArCH_3), 2.45 (1H, ddd, *J* 12.4, 6.1, 3.6, CH_2N), 2.63 (1H, ddd, *J* 12.4, 7.0, 3.7, CH_2N), 3.43 (1H, ddd, *J* 11.0, 6.2, 3.7, CH_2O), 3.48–3.54 (2H, m, C*H*NTs, CH_2O), 3.63 (1H, d, *J* 3.7, FurC*H*N), 4.59 (1H, b, N*H*), 6.14 (1H, d, *J* 3.1, Fur*H*), 6.30 (1H, dd, *J* 3.1, 1.9, Fur*H*), 7.28–7.36 (3H, m, Fur*H*, Ar*H*), 7.81 (2H, d, *J* 8.2, Ar*H*); δ_C 10.6 (CH_3), 21.5 (CH_3), 24.7 (CH_2), 49.2 (CH_2), 58.2 (CH), 58.8 (CH), 61.1 (CH_2), 108.1 (CH), 110.1 (CH), 127.1 (CH), 129.7 (CH), 138.4 (C_q), 142.2 (CH), 143.4 (C_q), 153.2 (C_q); *m/z* 353.1533 (MH$^+$, 100%, $C_{17}H_{24}N_2O_4S$ requires 353.1535).

N-[1-Ethyl-2-(2-hydroxy-ethylamino)-heptyl]-4-methyl-benzenesulfonamide (21b)

Synthesised in a similar manner to first **9** then **11**. Treatment of β-nitroamine **23b** (3.55 g, 11.8 mmol) with Al–Hg amalgam gave *O*-TMS protected hydroxylamine (2.81 g, 9.80 mmol, 83%) as a yellow oil that was passed through a plug of silica to give the desilylated hydroxylamine (1.59 g, 7.38 mmol, 63%, purity 90% by ^{1}H NMR) that slowly degraded at rt, IR ν_{max}/cm^{-1} 3500–3050 (O–H/N–H), 3000–2750 (C–H), 1464, 1379, 1108, 1064, 909, 733; δ_H 0.89 (3H, t, *J* 6.9, CH_2CH_3), 0.97 (3H, t, *J* 7.5, $CHCH_2CH_3$), 1.25–1.53 (10H, m, CH_2), 2.78 (1H, ddd, *J* 12.7, 6.4, 3.9, CH_2N), 2.80–2.84 (1H, m, C*H*NOH), 3.22 (2H, m, CH_2N/C*H*N), 3.64–3.71 (2H, m, CH_2O), 4.40 (1H, b, N*H*); δ_C 11.7 (CH_3), 14.1 (CH_3), 19.7 (CH_2), 22.6 (CH_2), 26.7 (CH_2), 30.5 (CH_2), 32.1 (CH_2), 50.0 (CH_2), 58.5 (CH), 61.5 (CH_2), 64.5 (CH); Compound was unstable to MS analysis.

Reduction of the hydroxylamine formed above (649 mg, 4.00 mmol) with $LiAlH_4$ gave 2-[1-(1-amino-propyl)-hexylamino]-ethanol (384 mg, 1.90 mmol, 40%, purity 90% by ^{1}H NMR) as an off white liquid that was unstable to chromatography and degraded at rt, IR ν_{max}/cm^{-1} 3400–3000 (O–H/N–H), 2960–2857 (C–H), 1464, 1378, 1115, 1065, 937, 733; δ_H 0.90 (3H, t, *J* 6.9, $CH_2CH_2CH_3$), 0.92 (3H, t, *J* 7.5, $CHCH_2CH_3$), 1.10–1.62 (10H, m, CH_2), 2.40–3.96 (4H, m, CH_2N/2 × C*H*N), 3.51–3.70 (2H, m, C*H*O); δ_C 11.4 (CH_3), 14.1 (CH_3), 22.7 (CH_2), 26.2 (CH_2), 30.2 (CH_2), 32.1 (CH_2), 32.2 (CH_2), 49.5 (CH_2), 54.6 (CH), 61.3 (CH_2), 61.9 (CH). Compound was unstable to MS analysis.

Tosylation of the primary amine of the diamine formed above (380 mg, 1.88 mmol) gave crude **21b** (724 mg, >95%) as a brown oil. Purification by flash chromatography (R_f = 0.59, 1 : 2 hexanes : EtOAc) gave pure **21b** (274 mg, 0.769 mmol, 41%) as a yellow oil, IR ν_{max}/cm^{-1} 3500–3100 (O–H/N–H), 2950–2850 (C–H), 1598 (N–H), 1327 (S=O), 1159 (S=O), 1094 (C–N); δ_H 0.79 (3H, t, *J* 7.4, $CHCH_2CH_3$), 0.89 (3H, t, *J* 7.2, $CH_2CH_2CH_3$), 1.10–1.43 (10H, m, CH_2), 2.21–2.29 (1H, m, C*H*NTs), 2.43 (3H, s, ArCH_3), 2.51 (1H, ddd, *J* 12.3, 5.4, 3.8, CH_2N), 2.73 (1H, ddd, *J* 12.3, 6.9, 4.2, CH_2N), 3.19 (1H, ddd, *J* 9.3, 5.1, 3.8, C*H*NCH_2), 3.53–3.57 (2H, m, CH_2O), 7.31 (2H, dd, *J* 8.5, 0.6, Ar*H*), 6.34 (2H,

dd, *J* 8.4, 0.8, Ar*H*); δ_C 10.8 (CH_3), 14.1 (CH_3), 21.6 (CH_3), 22.6 (CH_2), 22.8 (CH_2), 26.2 (CH_2), 30.8 (CH_2), 31.8 (CH_2), 49.4 (CH_2), 57.0 (CH), 59.8 (CH), 61.6 (CH_2), 127.1 (CH), 129.6 (CH), 138.3 (C_q), 143.2 (C_q); *m/z* 357.2201 (MH^+, 100%, $C_{18}H_{33}N_2O_3S$ requires 357.2212).

N-{1-[(2-Hydroxy-propylamino)-phenyl-methyl]-propyl}-4-methyl-benzenesulfonamide (21c)

Synthesised in a similar manner to first **9** then **11**. Treatment of β-nitroamine **23c** (2.83 g, 8.72 mmol) with Al–Hg amalgam gave *N*-{1-[phenyl-(2-trimethylsilanyloxy-propylamino)-methyl]-propyl}-hydroxylamine (2.30 g, 7.41 mmol, 85%) as a cloudy liquid, IR ν_{max}/cm^{-1} 3500–3150 (N–H/O–H), 2968–2877 (C–H), 1247 (Si–C), 837 (Si–C); δ_H ($CDCl_3$) 0.09 (9H, s, Si*Me*$_3$), 0.89 (3H, t, *J* 7.4, CH_2CH_3), 1.02 (1H, m, CH_2CH_3), 1.08 (3H, d, *J* 6.2, $CHCH_3$), 1.22 (1H, dqd, *J* 14.0, 7.4, 4.6, CH_2CH_3), 2.46 (1H, dd, *J* 11.6, 8.0, CH_2N), 2.52 (1H, dd, *J* 11.6, 3.5, CH_2N), 3.04–3.09 (1H, m, C*H*NOH), 3.88–3.94 (1H, m, C*H*O), 4.01 (1H, d, *J* 3.4, C*H*N), 7.21–7.35 (5H, m, Ar*H*); δ_C ($CDCl_3$) 0.3 (CH_3), 11.6 (CH_3), 20.6 (CH_2), 21.7 (CH_3), 55.2 (CH_2), 65.0 (CH_2), 66.4 (CH), 68.0 (CH), 127.3 (CH), 127.7 (CH), 128.5 (CH), 139.7 (C_q); *m/z* 311.2126 (MH^+, 100%, $C_{16}H_{31}N_2O_2Si$ requires 311.2149).

Reduction of the hydroxylamine formed above (2.28 g, 7.34 mmol) with $LiAlH_4$ gave a crude mixture of hydroxylamine, *O*-TMS-protected diamine and unprotected diamine (1.12 g) as a yellow oil. Purification by chromatography (hexanes : EtOAc) gave hydroxylamine (65 mg, 0.21 mmol, 3%), *O*-TMS-protected diamine (281 mg, 0.954 mmol, 13%) and unprotected diamine (720 mg, 3.25 mmol, 44%). Data for 1-(2-amino-1-phenyl-butylamino)-propan-2-ol; IR ν_{max}/cm^{-1} 3500–3100 (O–H/N–H), 3061–2876 (C–H), 1582 (N–H), 1118 (C–N); δ_H ($CDCl_3$) 0.98 (3H, t, *J* 7.4, CH_2CH_3), 1.12 (2H, d, *J* 6.2, $CHCH_3$), 1.10–1.20 (1H, m, CH_2CH_3), 1.58 (1H, dqd, *J* 13.7, 7.5, 4.0, CH_2CH_3), 2.33 (1H dd, *J* 12.2, 9.3, NCH_2), 2.55 (1H dd, *J* 12.2, 3.1, NCH_2), 2.89 (1H, ddd, *J* 8.9, 4.8, 4.1, C*H*NH$_2$), 3.63 (1H, d, *J* 4.9, C*H*Ph), 3.84 (1H, dqd, *J* 9.3, 6.2, 3.1, C*H*OH), 7.30–7.33 (3H, m, Ar*H*), 7.36–7.40 (2H, m, Ar*H*); δ_C ($CDCl_3$) 10.8 (CH_3), 20.5 (CH_3), 27.2 (CH_2), 54.3 (CH_2), 57.6 (CH), 65.5 (CH), 66.7 (CH), 127.2 (CH), 128.2 (CH), 128.3 (CH), 140.3 (C_q); *m/z* (EI$^+$) 223.1803 (MH^+, 90%, $C_{13}H_{23}N_2O$ requires 223.1805), 148 (100).

Tosylation of the primary amine a 3 : 1 mixture of hydroxy and *O*-TMS protected diamines (4.18 mmol) formed as above gave crude **21c** as a yellow oil (1.36 g, 3.61 mmol). Purification by flash chromatography ($R_f = 0.56$, 1 : 1 hexanes : EtOAc) gave pure **21c** (1.22 g, 3.24 mmol, 78%) as a highly viscous yellow oil, IR ν_{max}/cm^{-1} 3600–3400 (O–H), 3400–3200 (N–H), 2968–2877 (C–H), 1329 (S=O), 1161 (S=O), 1092 (C–N); δ_H ($CDCl_3$) 0.71 (3H, t, *J* 7.4, CH_2CH_3), 1.06 (3H, d, *J* 6.3, $CHCH_3$), 1.09–1.18 (1H, m, CH_2CH_3), 1.23–1.32 (1H, m, CH_2CH_3), 2.29 (1H dd, *J* 12.2, 8.8, NCH_2), 2.34 (1H dd, *J* 12.2, 3.4, NCH_2), 2.44 (3H, s, ArCH_3), 3.34–3.39 (1H, b, C*H*OH), 3.67 (1H, d, *J* 3.4, C*H*Ph), 3.70 (1H, ddd, *J* 8.9, 6.2, 3.4, C*H*NTs), 4.55 (1H, b, N*H*), 7.10–7.15 (2H, m, Ar*H*), 7.25–7.34 (5H, m, Ar*H*), 7.79–8.82 (2H, m, Ar*H*); δ_C ($CDCl_3$) 10.7 (CH_3), 20.6 (CH_3), 21.6 (CH_3), 23.4 (CH_2), 54.4 (CH_2), 60.2 (CH), 64.0 (CH), 66.0 (CH), 127.2 (CH), 127.6 (CH), 128.6 (CH), 129.7 (CH), 138.2 (C_q), 138.9 (C_q), 143.5 (C_q); *m/z* 377.1884 (MH^+, 100%, $C_{20}H_{29}N_2O_3S$ requires 377.1893).

N-{1-[(3-Hydroxy-propylamino)-phenyl-methyl]-propyl}-4-methyl-benzenesulfonamide (21d)

Synthesised in a similar manner to first **9** then **11**. Treatment of impure β-nitroamine **23d** (1.40 g, 85% conversion) with Al–Hg amalgam gave a 1 : 1 mixture of *O*-TMS protected hydroxylamine and deprotected hydroxylamine (1.03 g, 3.76 mmol) as a yellow oil. Purification by chromatography (hexanes : EtOAc) gave 3-(2-hydroxyamino-1-phenyl-butylamino)-propan-1-ol (520 mg, 2.05 mmol, 66%) as a pale yellow highly viscous oil, IR ν_{max}/cm^{-1} 3500–3027 (N–H/O–H), 2950–2870 (C–H), 1493, 1376, 1072 (C–N), 1028; δ_H 0.90 (3H, t, *J* 7.5, CH_2CH_3), 1.26 (1H, ddq, *J* 14.3, 9.1, 7.3, CH_2CH_3), 1.39 (1H, dqd, *J* 14.3, 7.6, 4.2, CH_2CH_3), 1.59–1.67 (1H, m, CH_2CH_2N), 1.73–1.83 (1H, m, CH_2CH_2N), 2.73–2.77 (2H, m, CH_2N), 3.03 (1H, dt, *J* 9.1, 4.1, C*H*NOH), 3.80–3.83 (2H, m, CH_2O), 4.05 (1H, d, *J* 4.1, C*H*N), 7.26–7.41 (5H, m, Ar*H*); δ_C 11.4 (CH_3), 20.1 (CH_2), 31.2 (CH_2), 47.3 (CH_2), 63.6 (CH_2), 64.3 (CH), 67.7 (CH_2), 127.1 (CH), 127.9 (CH), 128.6 (CH), 139.6 (C_q); *m/z* 239.1754 (MH^+, 100%, $C_{13}H_{23}N_2O_2$ requires 239.1754).

Reduction of the hydroxylamine formed above (520 mg, 2.05 mmol, 66%) with $LiAlH_4$ gave crude diamine (324 mg, 1.46 mmol, 39%) as a yellow oil. Purification by chromatography (hexanes : EtOAc) gave pure 3-(2-amino-1-phenyl-butylamino)-propan-1-ol (220 mg, 0.994 mmol, 27%) as a pale yellow highly viscous oil, IR ν_{max}/cm^{-1} 3500–3026 (N–H/O–H), 2932–2870 (C–H), 1601 (N–H), 1072 (C–N); δ_H 0.98 (3H, t, *J* 7.4, CH_2CH_3), 1.20–1.33 (1H, m, CH_2CH_3), 1.52–1.61 (1H, m, CH_2CH_3), 1.62–1.70 (1H, m, CH_2CH_2), 1.74–1.81 (1H, m, CH_2CH_2), 2.47–2.76 (3H, m, CH_2N/NH), 2.88–2.96 (1H, m, C*H*NH$_2$), 3.61 (1H, *J* 4.9, PhC*H*N), 3.80–3.87 (2H, m, CH_2O), 7.29–7.43 (5H, m, Ar*H*); δ_C 10.9 (CH_3), 27.1 (CH_2), 31.4 (CH_2), 47.1 (CH_2), 57.2 (CH), 63.4 (CH_2), 67.8 (CH), 127.2 (CH), 128.2 (CH), 128.4 (CH), 139.9 (C_q); *m/z* (EI$^+$) 223.1802 (MH^+, 100%, $C_{13}H_{23}N_2O$ requires 223.1805), 148 (61).

Tosylation of the primary amine of the diamine formed above (160 mg, 0.723 mmol) gave crude **21d** (233 mg, 0.594 mmol, 82%). Purification by flash chromatography ($R_f = 0.13$, 1 : 2 hexanes : EtOAc) gave pure **21d** (189 mg, 0.503 mmol, 70%) as an orange oil, IR ν_{max}/cm^{-1} 3600–3000 (N–H/O–H), 2970–2870 (C–H), 1598 (N–H), 1318 (S=O), 1160 (S=O), 1091 (C–N); δ_H 0.63 (3H, t, *J* 7.3, CH_2CH_3), 1.06–1.16 (1H, m, CH_2CH_3), 1.26–1.35 (1H, m, CH_2CH_3), 1.56–1.64 (1H, m, CH_2CH_2), 1.66–1.73 (1H, m, CH_2CH_2), 2.43 (3H, s, ArCH_3), 2.51–2.56 (1H, m, CH_2N), 2.66 (1H, ddd, *J* 11.1, 8.7, 4.4, CH_2N), 3.32–3.37 (1H, m, C*H*NTs), 3.49 (1H, b, N*H*), 3.72 (1H, m, C*H*Ph), 3.75–3.80 (2H, m, CH_2O), 7.17 (2H, d, *J* 7.5, Ar*H*), 7.25–7.38 (5H, m, Ar*H*), 7.80 (2H, d, *J* 8.1, Ar*H*); δ_C 10.8 (CH_3), 21.6 (CH_3), 23.4 (CH_2), 31.2 (CH_2), 46.9 (CH_2), 60.0 (CH), 63.5 (CH_2), 65.1 (CH), 127.2 (CH), 127.7 (CH), 128.7 (CH), 129.7 (CH), 137.9 (C_q), 138.4 (C_q), 143.5 (C_q); *m/z* 377.1883 (MH^+, 100%, $C_{20}H_{29}N_2O_3S$ requires 377.1893).

2-Ethyl-3-(furan-2-yl)-1-(toluene-4-sulfonyl)-piperazine (24a)

Synthesised in a similar manner to **13**, diamine **21a** (45 mg, 0.13 mmol) gave, after chromatography (silica), a 65 : 35 mixture of piperazine **24a**, and aziridine **25a** (29 mg, 0.086 mmol, 67%) as a pale yellow oil which could be separated by chromatography (alumina) to give pure piperazine **24a** (15 mg, 0.045 mmol, 35%)

a pale yellow oil [$R_f = 0.23$ (1 : 2 hexanes : EtOAc)]; IR ν_{max}/cm^{-1} 3329 (N–H), 2967–2875 (C–H), 1598 (N–H), 1333 (S=O), 1159 (S=O), 1092 (C–N); δ_H ($CDCl_3$) 0.72 (3H, t, *J* 7.5, CH_2CH_3), 1.16 (1H, dqd, *J* 14.4, 7.4, 4.6, CH_2CH_3), 1.27 (1H, b, NH), 1.68 (1H, ddq, *J* 14.4, 10.0, 7.5, CH_2CH_3), 2.43 (3H, s, $ArCH_3$), 2.68 (1H, td, *J* 12.4, 3.6, CH_2N), 2.90 (1H, ddd, *J* 12.2, 3.2, 1.3, CH_2N), 3.14 (1H, ddd, *J* 15.8, 12.6, 3.2, CH_2N), 3.73 (1H, ddt, *J* 14.2, 3.4, 1.3, CH_2N), 3.89 (1H, d, *J* 3.6, FurCHN), 3.89 (1H, dt, *J* 9.9, 4.0, CHNTs), 6.12 (1H, dt, *J* 3.3, 1.0, FurH), 6.31 (1H, dd, *J* 3.2, 1.9, FurH), 7.30–7.36 (3H, m, FurH, ArH), 7.78 (2H, d, *J* 8.3, ArH); δ_C ($CDCl_3$) 10.6 (CH_3), 17.6 (CH_2), 21.6 (CH_3), 40.5 (CH_2), 45.2 (CH_2), 56.4 (CH), 58.0 (CH), 105.6 (CH), 111.2 (CH), 127.1 (CH), 129.8 (CH), 139.0 (C_q), 141.6 (CH), 143.2 (C_q), 154 (C_q); *m/z* 335.1420 (MH^+, 100%, $C_{17}H_{22}N_2O_3S$ requires 335.1429).

N-{1-[Aziridin-1-yl-(furan-2-yl)-methyl]-propyl}-4-methyl-benzenesulfonamide (25a)

Synthesised in a similar manner to **14**, diamine **21a** (45 mg, 0.13 mmol) gave, after chromatography, a 65 : 35 mixture of aziridine **25a** and piperazine **24a** (33 mg, 0.098 mmol, 76%) as a yellow oil which could be separated by chromatography (alumina) to give aziridine **25a** (21 mg, 0.062 mmol, 48%) [$R_f = 0.23$ (1 : 2 hexanes : EtOAc)]; IR ν_{max}/cm^{-1} 3293 (N–H), 3062–2876 (C–H), 1599 (N–H), 1320 (S=O), 1161 (S=O), 1093 (C–N); δ_H ($CDCl_3$) 0.73 (3H, t, *J* 7.5, CH_2CH_3), 1.15 (1H, dd, *J* 7.2, 4.2, CH_2N), 1.22 (1H, dd, *J* 7.2, 4.1, CH_2N), 1.37–1.47 (2H, m, CH_2CH_3), 1.60–1.67 (2H, m, CH_2N), 2.43 (3H, s, $ArCH_3$), 2.63 (1H, d, *J* 3.6, FurCHN), 3.41 (1H, qd, *J* 6.9, 3.7, CHNTs), 5.03 (1H, d, *J* 6.5, NH), 6.25 (1H, dt, *J* 3.2, 0.7, FurH), 6.33 (1H, dd, *J* 3.2, 1.9, FurH), 7.28–7.31 (2H, m, ArH), 7.37 (1H, dd, *J* 1.9, 0.9, FurH), 7.81 (2H, d, *J* 6.5, ArH); δ_C ($CDCl_3$) 10.4 (CH_3), 21.6 (CH_3), 24.9 (CH_2), 26.1 (CH_2), 28.3 (CH_2), 58.7 (CH), 69.3 (CH), 108.3 (CH), 110.1 (CH), 127.5 (CH), 129.5 (CH), 137.8 (C_q), 142.4 (CH), 143.1 (C_q), 152.5 (C_q); *m/z* (EI^+) 335.1417 (MH^+, 100%, $C_{19}H_{25}N_2O_2S$ requires 335.1429), 292 (63).

2-Ethyl-3-pentyl-1-(toluene-4-sulfonyl)-piperazine (24b)

Synthesised in a similar manner to **13**, diamine **21b** (207 mg, 0.581 mmol) gave a 75 : 25 mixture of piperazine **24b** and aziridine **25b** (142 mg, 72%) as a yellow oil which could be separated by chromatography (silica) to give piperazine **24b** (100 mg, 0.292 mmol, 50%) as a yellow oil [$R_f = 0.17$ (1 : 1 hexanes : EtOAc)]; IR ν_{max}/cm^{-1} 3300 (N–H), 2957–2872 (C–H), 1343 (S=O), 1154 (S=O), 1091 (C–N); δ_H 0.89 (3H, t, *J* 7.2, $CH_2CH_2CH_3$), 0.90 (3H, t, *J* 7.4, $CHCH_2CH_3$), 1.14–1.33 (8H, m, CH_2), 1.40 (1H, dqd, *J* 14.3, 7.4, 4.2, $CHCH_2CH_3$), 1.70 (1H, ddq, *J* 14.4, 10.9, 7.0, $CHCH_2CH_3$), 2.42 (3H, s, $ArCH_3$), 2.49–2.54 (1H, m, CHNH), 2.54 (1H, td, *J* 12.4, 3.5, CH_2N), 2.75 (1H, dd, *J* 12.2, 2.0, CH_2N), 3.05 (1H, ddd, *J* 14.4, 12.7, 3.2, CH_2N), 3.62–3.67 (1H, m, CH_2N), 3.74 (1H, dt, *J* 7.2, 3.7, CHNTs), 7.28 (2H, d, *J* 8.4, ArH), 7.72 (2H, d, *J* 8.3, ArH); δ_C ($CDCl_3$) 10.7 (CH_3), 14.1 (CH_3), 16.2 (CH_2), 21.5 (CH_3), 22.5 (CH_2), 25.6 (CH_2), 31.9 (CH_2), 33.0 (CH_2), 40.9 (CH_2), 45.4 (CH_2), 57.7 (CH), 58.1 (CH), 127.0 (CH), 129.7 (CH), 139.3 (C_q), 142.9 (C_q); *m/z* 339.2085 (MH^+, 100%, $C_{18}H_{30}N_2O_2S$ requires 339.2106).

N-(2-Aziridin-1-yl-1-ethyl-heptyl)-4-methyl-benzenesulfonamide (25b)

Synthesised in a similar manner to **14**, diamine **21b** (207 mg, 0.581 mmol) gave a 25 : 75 mixture of piperazine **24b** and aziridine **25b** with the reaction byproducts PPh_3O and diethyl hydrazidodicarboxylate. Chromatography (silica) gave aziridine **25b** (26 mg, 0.077 mmol) as a 1 : 1 mixture with diethyl hydrazidodicarboxylate as a yellow oil [$R_f = 0.20$ (1 : 1 hexanes : EtOAc)], further purification by chromatography (alumina) led to degradation of the substrate, IR ν_{max}/cm^{-1} 3296 (N–H), 2956–2858 (C–H), 1599 (N–H), 1330 (S=O), 1160 (S=O), 1093 (C–N); δ_H ($CDCl_3$) 0.80 (3H, t, *J* 7.4, $CHCH_2CH_3$), 0.85 (3H, t, *J* 7.3, $CH_2CH_2CH_3$), 0.95–1.77 (14H, m, CH_2), 2.42 (3H, s, $ArCH_3$), 2.42–2.45, CHNH), 3.19 (1H, q, *J* 7.6, CHNTs), 5.32 (1H, d, *J* 7.7, NH), 7.29 (2H, d, *J* 8.8, ArH), 7.77 (2H, d, *J* 8.2, ArH); δ_C ($CDCl_3$) 10.1 (CH_3), 14.2 (CH_3), 14.5 (CH_3), 22.7 (CH_2), 24.8 (CH_2), 26.2 (CH_2), 26.5 (CH_2), 28.0 (CH_2), 31.5 (CH_2), 32.1 (CH_2), 57.8 (CH), 69.9 (CH), 127.0 (CH), 129.5 (CH), 138.8 (C_q); *m/z* 339.2089 (MH^+, 100%, $C_{18}H_{31}N_2O_2S$, requires 339.2106).

4-Methyl-*N*-{1-[(2-methyl-aziridin-1-yl)-phenyl-methyl]-propyl}-benzenesulfonamide (25c)

Synthesised in a similar manner to **13** or **14**, diamine **21c** (104 mg, 0.277 mmol) gave aziridine **25c** (34 mg, 0.094 mmol, 34%) [$R_f = 0.48$ (1 : 2 hexanes : EtOAc)]; IR ν_{max}/cm^{-1} 3293 (N–H), 3100–2875 (C–H), 1322 (S=O), 1160 (S=O), 1093 (C–N); δ_H ($CDCl_3$) 0.76 (3H, t, *J* 7.4, CH_2CH_3), 1.03 (3H, d, *J* 5.4, $CHCH_3$), 1.21–1.52 (4H, m, $CH_2CH_3/2 \times CH_2N/CHCH_3$), 1.55–1.64 (1H, m, CH_2CH_3), 2.46 (3H, s, $ArCH_3$), 2.69 (1H, d, *J* 3.4, CHPh), 3.35–3.43 (1H, m, CHNTs), 4.71 (1H, d, *J* 7.7, NH), 7.28–7.39 (7H, m, ArH), 7.83 (2H, d, *J* 8.3, ArH); δ_C ($CDCl_3$) 10.6 (CH_3), 18.0 (CH_3), 21.4 (CH_3), 23.7 (CH_2), 32.5 (CH), 36.6 (CH_2), 60.7 (CH), 75.9 (CH), 127.3 (CH), 128.0 (CH), 128.2 (CH), 129.4 (CH), 138.2 (C_q), 140.0 (C_q), 143.0 (C_q); *m/z* 359.1792 (MH^+, 100%, $C_{20}H_{27}N_2O_2S$ requires 359.1788).

2-Ethyl-3-phenyl-1-(toluene-4-sulfonyl)-1,4-diazepane (24d)

Synthesised in a similar manner to **13**, diamine **21d** (100 mg, 0.270 mmol) gave 1,4-diazepane **24d** (69 mg, 0.191 mmol, 71%) as a pale yellow oil [$R_f = 0.41$ (2 : 1 hexanes : EtOAc)]; IR ν_{max}/cm^{-1} 3340 (N–H), 3061–2876 (C–H), 1598 (N–H), 1332 (S=O), 1155 (S=O), 1089 (C–N); δ_H ($CDCl_3$) 0.31 (3H, t, *J* 7.4, CH_2CH_3), 1.14 (1H, dqd, *J* 14.8, 7.5, 4.1, CH_2CH_3), 1.58 (1H, ddq, *J* 14.8, 11.2, 7.4, CH_2CH_3), 1.77–1.92 (1H, m, CH_2CH_2N), 2.05–2.14 (1H, m, CH_2CH_2N), 2.41 (3H, s, $ArCH_3$), 2.84 (1H, ddd, *J* 13.6, 10.7, 4.6, CH_2NTs), 3.11 (1H, ddd, *J* 14.8, 7.0, 6.8, CH_2NH), 3.23 (1H, ddd, *J* 13.6, 6.1, 3.5, CH_2NTs), 3.78 (1H, ddd, *J* 14.9, 7.9, 4.3, CH_2NH), 3.96 (1H, dt, *J* 11.2, 3.6, CHNTs), 4.10 (1H, d, *J* 3.2, PhCHN), 7.22–7.35 (7H, m, ArH), 7.77 (2H, d, *J* 8.2, ArH); δ_C ($CDCl_3$) 10.8 (CH_3), 17.1 (CH_2), 21.5 (CH_3), 30.6 (CH_2), 40.1 (CH_2), 47.5 (CH_2), 64.6 (CH), 70.6 (CH), 126.8 (CH), 127.1 (CH), 128.4 (CH), 129.5 (CH), 138.6 (C_q), 142.0 (C_q), 142.9 (C_q); *m/z* (EI^+) 359.1788 (MH^+, 100% $C_{20}H_{26}N_2O_2S$ requires 359.1793), 212 (12).

***N*-{1-[(3-Chloro-propylamino)-phenyl-methyl]-propyl}-4-methyl-benzenesulfonamide**

Synthesised in a similar manner to **14**, diamine **21d** (90 mg, 0.24 mmol), gave chloride (86 mg, 0.22 mmol, 92%), as a yellow oil [R_f = 0.48 (2 : 1 hexanes : EtOAc)]; IR ν_{max}/cm^{-1} 3288 (N–H), 2969–2874 (C–H), 1598 (N–H), 1334 (S=O), 1161 (S=O), 1092 (C–N); δ_H ($CDCl_3$) 0.77 (3H, t, *J* 7.3, CH_2CH_3), 1.10–1.21 (1H, m, CH_2CH_3), 1.24–1.33 (1H, m, CH_2CH_3), 1.82 (2H, p, *J* 6.6, $CH_2CH_2CH_2$), 2.36 (1H, dt, *J* 11.9, 6.6, CH_2N), 2.47 (3H, s, $ArCH_3$), 2.62 (1H, dt, *J* 11.9, 6.6, CH_2N), 3.35 (1H, b, CHNTs), 3.54–3.64 (3H, m, CH_2Cl, CHPh), 4.94 (1H, bd, *J* 8.5, NH), 7.11 (2H, dd, *J* 8.3, 1.2, ArH), 7.26–7.39 (5H, m, ArH), 7.86 (2H, bd, *J* 8.3, ArH); δ_C ($CDCl_3$) 10.7 (CH_3), 21.6 (CH_3), 23.0 (CH_2), 32.9 (CH_2), 43.0 (CH_2), 44.4 (CH_2), 60.1 (CH), 64.6 (CH), 127.2 (CH), 127.3 (CH), 127.5 (CH), 128.6 (CH), 129.8 (CH), 138.3 (C_q), 139.1 (C_q), 143.5 (C_q); *m/z* 395.1550 (MH^+, 100%, $C_{20}H_{28}ClN_2O_2S$ requires 395.1555).

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