Generation of homochiral aziridinium ion intermediates derived from 2,3-epoxy amines: regiospecific nucleophilic trapping with nitrogen nucleophiles. Application in the synthesis of novel morpholino-sphingolipid analogues with potential glucosylceramide synthase inhibitory activity

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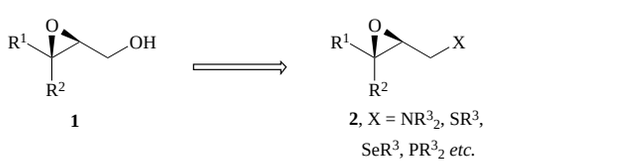
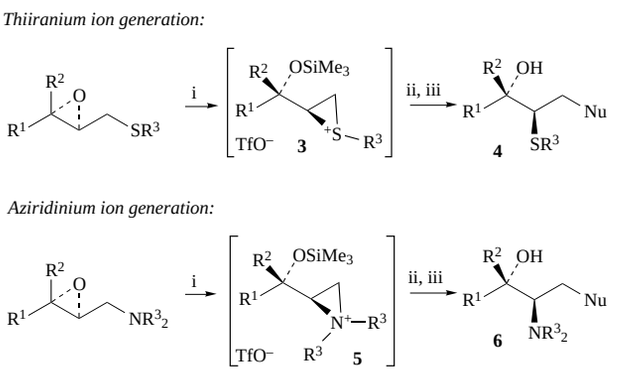
The Lewis acid induced rearrangement of 2,3-epoxy amines into the corresponding 2-trimethylsilyloxymethylaziridinium ions is described. Such intermediates have been characterised by ^{1}H NMR spectroscopy, and react with nitrogen nucleophiles regiospecifically to form 1-substituted 2,3-amino alcohols in good to excellent yields and with full stereochemical control. This methodology has been applied to the synthesis of a potential inhibitor of glucosylceramide synthase, a promising target for cancer chemotherapy.

Introduction

The Sharpless asymmetric epoxidation (SAE) is one of the most useful asymmetric reactions available to the synthetic chemist.[1] In particular, the generality of the reaction allows for the preparation of a wide variety of homochiral 2,3-epoxy alcohols which are extremely useful synthetic intermediates.[2] Some time ago, we initiated a research programme to investigate the chemistry of derivatives of 2,3-epoxy alcohols **1** where the oxygen atom of the alcohol group is replaced by a different heteroatom **2**.





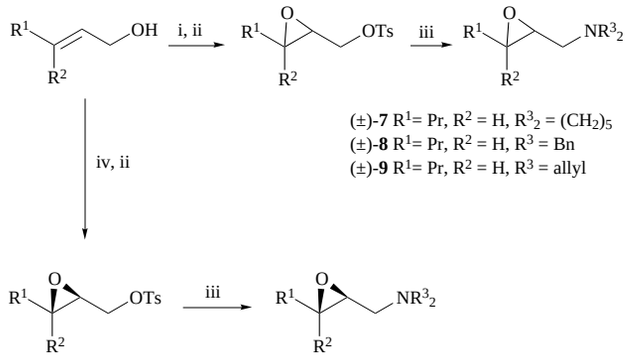
Scheme 1 *Reagents and conditions:* i, Lewis acid (*e.g.* TMSOTf); ii, nucleophile (Nu); iii, desilylation

Our initial work centred on 2,3-epoxy sulfides for which we have developed synthetic routes to 2,3-epoxy sulfoxides, 2,3-dihydroxy sulfoxides, and (*E*)-γ-hydroxy-α,β-unsaturated sulfoxides and sulfones.[3] They can also be used to prepare homochiral β-hydroxy sulfides **4** by regiospecific nucleophilic trapping of thiiranium ion intermediates **3**, generated *in situ* from the 2,3-epoxy sulfides under Lewis acidic conditions.[4] This work provided the basis for an extension of this methodology to the corresponding 2,3-epoxy amine systems described here.[5] Thus under Lewis acidic conditions we envisaged that a 2,3-epoxy amine containing a tertiary amine group would undergo transformation into a reactive aziridinium ion **5** which could be opened with nucleophiles to form substituted β-amino alcohols **6** (Scheme 1). Although aziridinium ions are well established intermediates, primarily as a result of their biological activity,[6] their use in synthesis has been much less extensively studied.[7] This paper describes in detail our work on the generation and characterisation of novel homochiral aziridinium ion intermediates, and their regiospecific nucleophilic trapping with some nitrogen-based nucleophiles. The product amino alcohols have potential as chiral ligands in asymmetric synthesis,[8] as novel biologically active compounds[9] and as new systems capable of self organisation *via* hydrogen bonding.[10] We also describe how we have applied this methodology for the synthesis of a novel morpholinosphingolipid analogue with potential glucosylceramide synthase inhibitory activity, a promising target for cancer chemotherapy.[11]

Synthesis of 2,3-epoxy amine substrates

The required 2,3-epoxy amines are readily prepared from the corresponding 2,3-epoxy alcohols by tosylation and KI catalysed displacement using a secondary amine nucleophile (Scheme 2).[12] Some of the 2,3-epoxy alcohols have been described previously[3,4,13] and the remainder were prepared using relatively straightforward or known procedures. They were initially prepared as the racemate by $VO(acac)_2$ catalysed epoxidation using *tert*-butyl hydroperoxide (TBHP), however this gave only a poor yield of the *cis*-epoxy alcohols. Fortunately, the conventional SAE proved much more general giving good yields of all epoxy alcohols of high enantiomeric excess.[4]

For our initial studies we chose the simple *trans*- and *cis*-2,3-epoxy amines **7**–**12**[5] as representative substrates to investigate the effect of epoxide geometry and the nature of the amine on the rearrangement reaction. Note that tertiary amines are



Scheme 2 *Reagents and conditions:* i, $VO(acac)_2$, TBHP, CH_2Cl_2 (95%); ii, TsCl, pyridine (73–93%); iii, $R^3{}_2NH$, KI, DMF (75–92%); iv, $Ti(OPr^i)_4$, (+)-DET, TBHP, CH_2Cl_2 (57–84%)

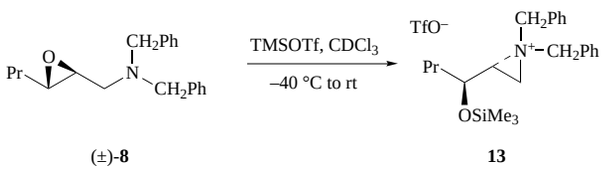
required for aziridinium salt formation, and that the diallyl- and dibenzyl-amines are of particular importance as they will allow ready deprotection[14] to the corresponding primary amines, which are in many cases our desired target molecule.

Generation of aziridinium ions

The conversion of **8** to **13** is related to the known Payne rearrangement of 2,3-epoxy alcohols[15] where an equilibrium mixture of isomeric epoxy alcohols is produced resulting from base catalysed intramolecular nucleophilic ring opening of the epoxide by the adjacent alkoxide.[16] A recent paper has described a related conversion of a primary 2,3-epoxy amine to the corresponding aziridinyl alcohol using trimethylaluminium as catalyst.[17] Similarly, 1,2-epoxy-3-sulfonamides are reported to rearrange under basic conditions[18] to the *N*-tosylaziridine-2-methanols which can be reacted with suitable nucleophiles.[19] The Payne rearrangement–nucleophilic trapping procedure[16] is a particularly important adaptation of the reaction, where the most reactive epoxide isomer (usually a terminal epoxide) is trapped by reacting with a nucleophile selectively at the more reactive primary epoxide position, thus displacing the epoxide equilibrium. In our case, we believed that under Lewis acid conditions, it should be possible to convert our epoxy amines to the desired aziridinium salts rather than producing an equilibrium mixture. It should then be possible to add a nucleophile to trap the reactive aziridinium ion intermediate in the reaction. Note that this entire synthetic sequence would be expected to be a stereospecific process and so, when used in conjunction with the SAE, would allow full control of relative and absolute stereochemistry.

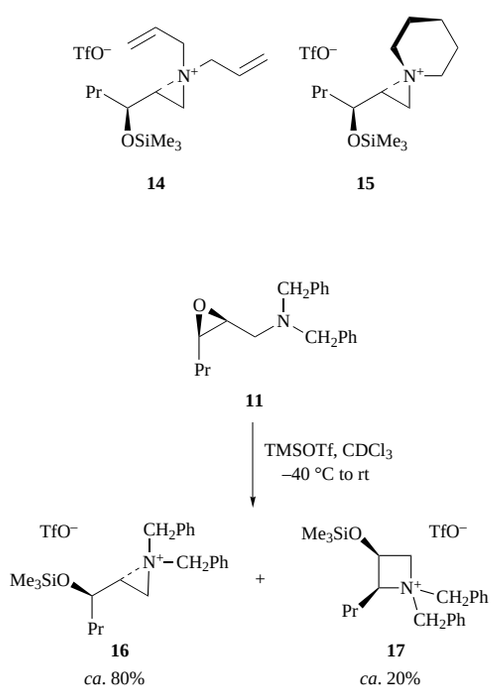
Efficient methods for the generation of aziridinium salts rely on essentially two approaches, either the addition of diazomethane to an iminium ion,[20] or neighbouring group participation by a tertiary amine adjacent to a centre with a good leaving group. The latter is by far the most common method and is particularly relevant to this work. In many previous examples where aziridinium salts have been used, they have been present only in a small equilibrium concentration;[21] however this equilibrium can be displaced by, for example, the use of Ag^I.[22] We believed it to be important that the generation of the aziridinium salt was irreversible for our systems to prevent the formation of products related to piperazinium dimers, which are often side products when aziridinium salts are generated from β-halo amines.[23] This dimerisation has been shown to be the dominant reaction even in the presence of nucleophiles including amines and amino acids; however we have not observed any related side reactions using our new protocol (*vide infra*).

With our substrates in hand, we thus began to investigate aziridinium salt formation. The 2,3-epoxy amine **8**, derived from dibenzylamine, was treated with trimethylsilyl trifluoromethanesulfonate (TMSOTf) in $CDCl_3$ at −40 °C and the reaction allowed to warm to room temperature (Scheme 3). The



Scheme 3

^{1}H NMR spectrum of the resulting solution clearly showed clean formation of the aziridinium salt **13**, which was stable for a number of days at room temperature. Only a single diastereoisomeric aziridinium salt was formed, consistent with the expected stereospecificity of the rearrangement process. This was also the case for a variety of other substrates, including the diallylamine **9** and piperidine **7** systems, resulting in clean formation of **14** and the spiro aziridinium salt **15** respectively. In the case of the *cis*-epoxy amines, although the major component of the reaction mixture was the desired aziridinium ion intermediate, the reaction was not as clean, even when carried out at −78 °C in CH_2Cl_2, or using *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBDMSOTf) in place of TMSOTf. We believe that in these cases, the by-product is actually the corresponding azetidinium salt **17** resulting from non-regioselective epoxide opening (Scheme 4) although this result

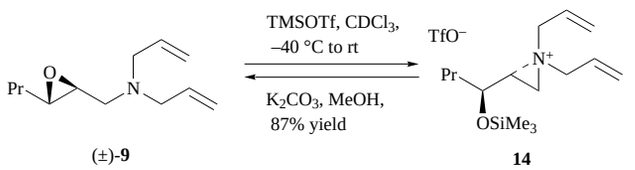


Scheme 4

requires further confirmation. It may also account for reduced yields being observed for nucleophilic trapping procedures involving some *cis*-2,3-epoxy amines (*vide infra*). It was clear from these results that, in most cases, we indeed had the desired quantitative aziridinium salt formation, rather than any equilibrium process as would be the case in a conventional Payne rearrangement, and this encouraged us to investigate the *in situ* nucleophilic trapping process (next section).

One further interesting point to note about this reaction is

that it can actually be reversed if necessary simply by deprotection of the trimethylsilyl group under basic conditions (Scheme 5). In some cases, after attempted trapping with reagents such



(±)-**9** **14**

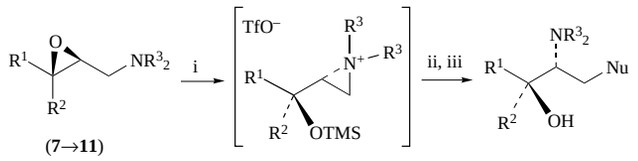
Scheme 5

as TMSCN, which were unsuccessful presumably due to their low nucleophilicity (although we had observed quantitative aziridinium salt formation initially), only the original 2,3-epoxy amine was isolated in the product mixture after the conventional work-up with K_2CO_3 in MeOH. We reasoned that this may indicate that formation of the aziridinium salt was reversible under suitable reaction conditions. To investigate this, the diallylamine derived epoxy amine **9** was treated with TMSOTf in $CDCl_3$ at −40 °C, and quantitative aziridinium salt formation observed by NMR spectroscopy. The salt was then subjected to our standard deprotection conditions (K_2CO_3–MeOH) and the original *trans*-2,3-epoxy amine starting material was generated in good yield, presumably by intramolecular ring opening of the aziridinium ring by the adjacent alkoxide produced during desilylation. This was a stereospecific process as would be expected, and no products of intermolecular nucleophilic ring opening by methoxide were observed. We are currently investigating the scope of this reaction further in aziridinium salt chemistry, and it also has possible implications for our related work using 2,3-epoxy sulfides (*cf.* Scheme 1) as in some cases considerable amounts of starting material could be recovered from the crude product mixture of attempted nucleophilic trappings of the thiiranium ion intermediates, although we have so far been unable to prove initial quantitative thiiranium ion formation.[4]

Nucleophilic trapping of aziridinium ions

Aziridines are readily accessible synthetic intermediates[24] but are under-used in synthesis, particularly when compared with epoxides. This is probably due to their limited synthetic accessibility, and their relatively low reactivity, often requiring a strong electron withdrawing group on the nitrogen atom to promote ring opening with nucleophiles.[25] Examples where aziridinium salts have been used in synthesis are also relatively rare;[7] however their enhanced reactivity, particularly when compared to aziridines, make them potentially extremely useful electrophiles, particularly for reaction with relatively weak nucleophiles.[25] An alternative and potentially very attractive method of activating aziridines toward nucleophilic ring opening is by the use of protic acid catalysis.[26] This, however greatly restricts the types of nucleophiles which can be used, ruling out most organometallic reagents (organo-lithium, -copper and -magnesium). In addition, for simple amine nucleophiles (pK_a *ca.* 10–11),[27] the reduced basicity of aziridines (aziridine pK_a 7.98)[28] also means that simple acid catalysis is likely to be unsuccessful due to unfavourable *N*-protonation equilibria between the two reactants. For these reasons we decided to investigate peralkyl substituted aziridinium salts containing groups which could be readily removed under mild reaction conditions, to yield primary amines, which are often our desired target (*vide infra*).

The real advantage of our procedure is if the aziridinium intermediates can be efficiently trapped with nucleophiles, under mild reaction conditions, particularly with poor nucleophiles which have proved problematic previously. The results of our investigations are shown in Table 1. Treatment of the 2,3-epoxy amine with TMSOTf at −78 °C in dichloromethane generates the required aziridinium salt as described above

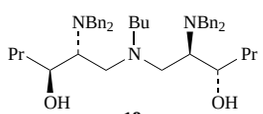


(**7**→**11**)

Scheme 6 *Reagents and conditions:* i, TMSOTf (1.2 equiv.), CH_2Cl_2, −78 °C, 10 min; ii, nucleophile, −78 °C→room temp., 3–5 days; iii, K_2CO_3, MeOH, room temp., 45 min

(Scheme 6). Addition of an appropriate nucleophile, warming to room temperature, and stirring for up to 5 days gives good to excellent yields of our desired products. In general, the initially formed trimethylsilyl ethers were deprotected without isolation, and quoted yields are for the three step process of aziridinium salt formation, nucleophilic trapping and deprotection. Of particular importance is the high regioselectivity of the reaction, which results in introduction of the nucleophile exclusively at the less hindered terminal carbon (C-1). The reaction is successful for all the 2,3-epoxy amine substrates so far investigated, and is also stereospecific. Optical activity is retained in the products as would be expected from the intermediacy of the aziridinium salt and the stereospecificity of the processes (entries 3, 5, 11 and 12).

A variety of nitrogen based nucleophiles were used including aromatic heterocycles, and cyclic and acyclic secondary amines. Primary amines such as butylamine could also be used although small amounts of side products resulting from bis-*N*-alkylation **18** were obtained. With more hindered primary



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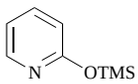
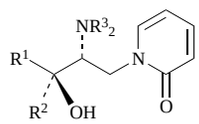
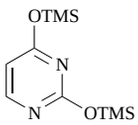
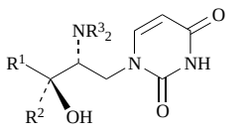
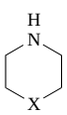
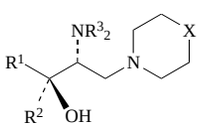
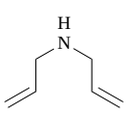
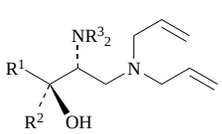
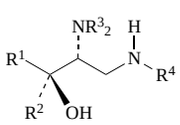
amines such as isopropylamine, no products of polyalkylation were observed although yields were only moderate. Interestingly, the use of liquid ammonia at low temperature (−33 °C) gave only the product of monoalkylation. Note that in the case of the piperidine derived 2,3-epoxy amine (entry 7), we found it necessary to resort to using TBAF for deprotection of the initially formed trimethylsilyl ether. The reason for this is interesting in that although deprotection using K_2CO_3–MeOH proceeded without apparent incident, it proved impossible to obtain a satisfactory elemental analysis consistent with the product. The observed elemental analysis actually calculated approximately to a 1:1 complex between the product and K_2CO_3. Although this is perhaps not surprising as amino alcohols are well known to coordinate to metals,[8] it is unclear at present why this is the only case where this phenomenon was observed. Fortunately, use of TBAF in the deprotection step induced rapid desilylation, and the final product gave a satisfactory elemental analysis.

One of our most successful nucleophilic trapping reagents was bis(*O*-trimethylsilyl)uracil (entries 4, 5 and 6). Our other interests in nucleoside chemistry[29,30] led us to consider the synthesis of related systems with complementary hydrogen bonding properties, which will have applications in areas such as antisense oligonucleotides and supramolecular chemistry. With this in mind, the product of aziridinium opening with ammonia was reacted with the chloropyrimidine **20** in MeCN to give the product **21** (Scheme 7) which has complementary hydrogen bonding properties to uracil. Preliminary studies (^{1}H NMR) indicate that, in $CDCl_3$ the two monomers associate by hydrogen bonding to form **23** and **24**. We are currently further investigating such aggregation phenomena, along with developing new methods for the introduction of other nucleoside bases in related systems, the details of which will be published in due course.[30]

Table 1 Results of nucleophilic trapping of aziridinium salts

Entry	Substrate[a]	Nucleophile	Product		Yield (%)
1	**8**				93
2	**9**				83
3	**10**				79[b]
4	**8**				89
5	**9**				91[b]
6	**7**				79[c]
			11		
7	**8**			X = CH_2	60
8	**9**			X = CH_2	66
9	**8**			X = O	92
10	**9**			X = O	90
11	**10**			X = O	59[b]
12	**11**			X = O	58[b]
13	**8**				67
14	**9**				89
15	**8**	$BuNH_2$		R^4 = Bu	44[d]
16	**8**	Pr^iNH_2		R^4 = Pr^i	47
17	**9**	Pr^iNH_2		R^4 = Pr^i	47
18	**8**	NH_3 (liq.)		R^4 = H	65[e]
19	**9**	NH_3 (liq.)		R^4 = H	54[e]

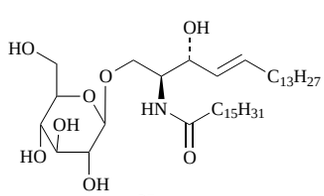
[a] All compounds used as racemates unless otherwise stated. [b] Optically active 2,3-epoxy amine used. [c] TBAF used in deprotection rather than K_2CO_3 (see text). [d] 12% bis-alkylated product also isolated. [e] Only monoalkylated product isolated.

Synthesis of a potential inhibitor of glucosylceramide synthase

Glucosylceramide **25** (glucocerebroside, 1-*O*-β-D-glucopyranosylceramide) is widely distributed in normal and pathologenic tissue, including normal human serum,[31] plasma,[32] erythrocytes,[33] kidney[34] and aortic tissue,[35] as well as in the central nervous system.[36] It is the major cerebroside found in the spleen of patients with Gaucher's disease.[37] The biosynthesis of glucosylceramide relies on the coupling of UDP-glucose to C-1 of an *N*-acylsphingosine (ceramide) mediated by glucosylceramide synthase, and inhibition of this process is a promising target for cancer chemotherapy.[11,38]

Glucosylceramide is also hydrolysed by a glucosidase to ceramide and glucose.[38] In the human genetic disorder Gaucher's disease, the glucosidase is inefficient and glucosylceramide accumulates. Administering an inhibitor of the glucosylceramide synthase to individuals with this disease would slow the formation of glucosylceramide to a rate matching their hydrolytic capability and prevent further accumulation of the lipid.[39] Therefore, a variety of compounds resembling *N*-acylsphingosine (ceramide) and glucosylceramide have been investigated in an attempt to block the glucosylceramide synthesis.

Based on earlier investigations,[39,40] compound **26** has recently been reported as being a particularly powerful inhibitor of glucosylceramide synthase,[11] with the (*R*,*R*)-stereoisomer being the most active. Our new methodology allows ready access to morpholine-substituted amino alcohols such as **26**, although we decided on our initial target **27** which we considered to be a suitable isostere for **26**.



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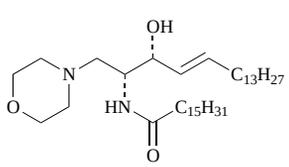

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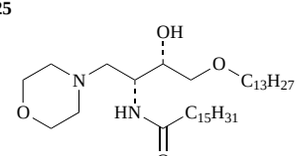
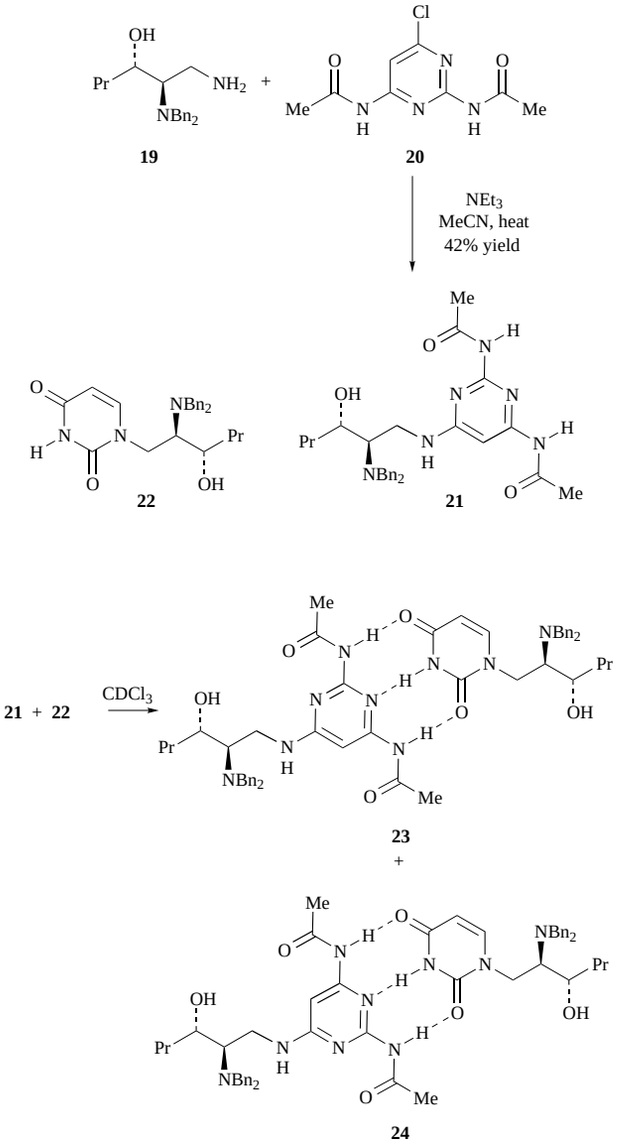


27

The primary challenge of the synthesis of **27** is the control of relative and absolute stereochemistry. With our methodology, this is established by choice of the (+)-diethyl tartrate in the SAE, and using the (*Z*)-configured allylic alcohol. We also wanted to develop a route which was flexible enough to allow the synthesis of other analogues such as **26** and related systems to provide an opportunity to investigate the structure–activity relationship of the inhibitors of glucosylceramide.



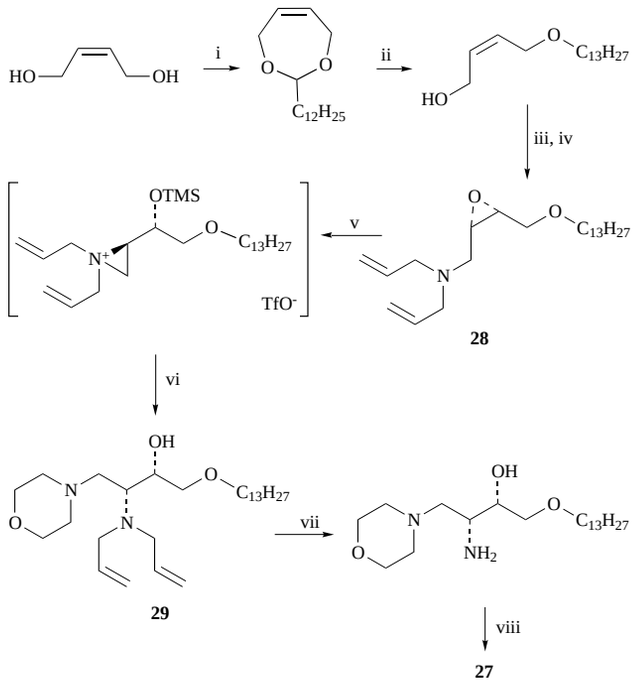
Scheme 7

The synthetic route is outlined in Scheme 8. Commercially available *cis*-but-2-ene-1,4-diol was selectively mono-*O*-alkylated by a two-step procedure incorporating AlH_3 mediated acetal reduction.[41] Subsequent SAE of the (*Z*)-allylic alcohol gave the desired 2,3-epoxy alcohol (86% ee) which was converted into the corresponding diallylamine **28** using established procedures (*vide supra*). The aziridinium salt derived from **28** was then generated under conventional conditions (TMSOTf, −78 °C), and trapped with morpholine. Deprotection using potassium carbonate and methanol gave the diallyl-protected amino alcohol **29** in 61% overall yield from **28**.

Removal of the *N*-allyl groups of **29** proved problematic. Under conditions previously successful for accomplishing this transformation[5a] using $(Ph_3P)_3RhCl$–MeCN–H_2O[14a]; only very low yields of the desired product were obtained, possibly due to problems of solubility and/or metal chelation. However a modified procedure[14b] using Pd/C, methanesulfonic acid, and water gave the desired primary amine in 82% yield. Final *N*-acylation using 4-nitrophenyl palmitate[42] gave the desired product **27** which is currently undergoing biological testing, the results of which will be reported at a later date.

Conclusions

In summary, this powerful new methodology provides access to a range of 1-substituted 2,3-amino alcohols with full control of absolute and relative stereochemistry. We are currently applying



Scheme 8 *Reagents and conditions:* i, $C_{12}H_{25}CHO$, TsOH, C_6H_6, heat (98%); ii, $AlCl_3$, $LiAlH_4$, Et_2O (91%); iii, $Ti(OPr^i)_4$, (+)-DET, TBHP, CH_2Cl_2 (76%); iv, TsCl, pyridine (70%); $(allyl)_2NH$, KI, DMF (81%); v, TMSOTf, CH_2Cl_2, −78 °C; vi, morpholine, −78 °C→rt; K_2CO_3, MeOH (61%); vii, Pd/C, $MeSO_3H$, H_2O (82%); viii, *p*-nitrophenyl palmitate, pyridine (63%)

this new methodology to the synthesis of new chiral ligands for asymmetric catalysis, novel biologically active compounds, and new systems capable of self organisation *via* hydrogen bonding. The results of these studies will be reported in due course.

Experimental

General procedures and instrumentation

Melting points were determined on a Reichert hot stage apparatus and are uncorrected. Nuclear magnetic resonance spectra were recorded at 300 MHz for ^1H and 75 MHz for ^{13}C on a General Electric QE 300 spectrometer, and at 250 MHz for ^1H on a Bruker AM 250 spectrometer. Chemical shifts are expressed in parts per million (ppm) downfield of tetramethylsilane for ^1H resonances, and referenced to the central peak of the deuteriated chloroform triplet for ^{13}C resonances.

Infrared spectra were recorded on a Philips PU 8706 infrared spectrophotometer and signals were referenced to the polystyrene 1601 cm^{-1} absorbtion. Mass spectra were recorded on a VG Autospec mass spectrometer. Optical rotations were measured on an Optical Activity AA-1000 polarimeter, calibrated using a solution of camphor in ethanol of known rotation, $[\alpha]_D^{20}$ +44.1 (*c* 10, ethanol) and given in units of 10^{-1} deg cm^2 g^{-1}. Microanalyses were carried out at Leeds University Microanalytical Laboratory.

Thin layer chromatography was carried out using precoated aluminium-backed silica plates which were visualised using ultraviolet light and permanganate stain. Flash chromatography signifies column chromatography on Merck silica gel (230–400) or equivalent according to the method of Still.[43]

All glassware was washed with acetone, oven dried overnight at 125 °C and allowed to cool under a stream of dry nitrogen prior to use. Reactions were carried out under a positive pressure of dry oxygen-free nitrogen. Solvents were removed under reduced pressure using a Buchi rotary evaporator at water aspirator pressure, followed by drying under high vacuum at 0.5 mmHg.

Solvents were purified prior to use by established procedures[44] and other reagents used as received. Light petroleum refers to

the fraction with bp 40–60 °C unless otherwise stated. Toluene-*p*-sulfonyl chloride was purified prior to use by recrystallisation from light petroleum. Hexamethyldisilazane was purified prior to use by distillation. 10% Palladium on charcoal was supplied by Avocado Research Chemicals Ltd. Trimethylsilyl trifluoromethanesulfonate was obtained from the Aldrich Chemical Company Ltd. and used immediately upon opening. Solutions of *tert*-butyl hydroperoxide were prepared and standardised according to the method of Sharpless.[1a] The following compounds were synthesised using literature procedures: (±)- and (−)-(2*S*,3*S*)-3-propyloxirane-2-methanol,[1a,3] (−)-(2*S*,3*R*)-3-propyloxirane-2-methanol,[45] *O*-trimethylsilyl-2-pyridone,[46] bis-(*O*-trimethylsilyl)uracil,[47] (*E*)-but-2-ene-1,4-diol[48] and (*E*)-4-*tert*-butyldimethylsilyloxybut-2-en-1-ol.[13] Enantiomeric excesses of epoxy alcohols were determined by ^{1}H NMR spectroscopy using Eu(hfc)$_3$ on the corresponding acetate derivatives.

Synthesis of 2,3-epoxy amine substrates and precursors

(−)-(2*S*,3*S*)-1-(*N*,*N*-Diallylamino)-4-*tert*-butyldimethylsilyloxy-2,3-epoxybutane (−)-10

(2*S*,3*S*)-3-(*tert*-Butyldimethylsilyloxymethyl)oxirane-2-methanol.[42] A procedure similar to (−)-(2*S*,3*S*)-3-propyloxirane-2-methanol[1a,3] using (*E*)-4-*tert*-butyldimethylsilyloxybut-2-en-1-ol (10.1 g, 50.2 mmol), titanium isopropoxide (14.3 g, 15.0 cm^3, 50.2 mmol), L-(+)-diethyl tartrate (10.4 g, 8.60 cm^3, 50.2 mmol), *tert*-butyl hydroperoxide (39.1 cm^3, 100 mmol, 2.57 mol dm^{-3} in toluene), ferrous sulfate (25 g) and tartaric acid (19 g) in water (187 ml) and NaOH (6.2 g) in brine (167 ml) gave the crude product which was purified by column chromatography on flash silica (eluent 1:3 ethyl acetate–light petroleum) to give (2*S*,3*S*)-3-(*tert*-butyldimethylsilyloxymethyl)oxirane-2-methanol (9.19 g, 42.2 mmol, 84%) as a colourless liquid; $[\alpha]_D^{21}$ −12.2 (*c* 1.05 in MeOH) {lit., $[\alpha]_D^{24}$ −11.6 [*c* 0.9 in MeOH]};[42] δ_H(300 MHz; $CDCl_3$) 0.08 [6 H, s, Si(CH$_3$)$_2$], 0.91 [9 H, s, C(CH$_3$)$_3$], 1.80 (1 H, br, OH), 3.12–3.16 (2 H, m, 2-H, 3-H), 3.65 (1 H, dd, *J* 12.0, 4.0, one of CH$_2$OTBDMS), 3.72 (1 H, dd, *J* 12.0, 4.0, one of CH$_2$OTBDMS), 3.89 (1 H, dd, *J* 12.5, 3.0, one of C*H*$_2$OH), 3.98 (1 H, dd, *J* 12.5, 4.0, one of C*H*$_2$OH); δ_C(75 MHz; $CDCl_3$) −5.50 [2 C, Si(CH$_3$)$_2$], 18.18 (*C*Me$_3$), 25.69 [3 C, C(*C*H$_3$)$_3$], 55.56 (2-C or 3-C), 55.71 (2-C or 3-C), 61.12, 62.48; ν_{max}(thin film)/cm^{-1} 3500–3280 (br, m), 2940 (s), 2920 (s), 2870 (m), 2840 (s), 1735 (w), 1460 (m), 1380 (w), 1355 (w), 1250 (s), 1100 (s), 995 (w), 985 (w), 930 (w), 860 (w), 830 (s), 770 (s); *m/z* (EI) 219 (M$^+$ + 1, 25%), 203 (39), 189 (22), 185 (7), 161 (23), 143 (12), 127 (11), 117 (76), 105 (9), 101 (15), 89 (27), 84 (24), 75 (100), 69 (9), 59 (31), 45 (11), 41 (29) (Found C, 54.95; H, 10.15. Calc. for $C_{10}H_{22}O_3Si$: C, 55.05; H, 10.09%).

(−)-(2*S*,3*S*)-3-(*tert*-Butyldimethylsilyloxymethyl)oxiran-2-ylmethyl 4-methylbenzenesulfonate. A procedure similar to (±)-(2*S**,3*S**)-3-propyloxiran-2-ylmethyl 4-methylbenzenesulfonate[4] using (2*S*,3*S*)-3-(*tert*-butyldimethylsilyloxymethyl)-oxirane-2-methanol (5.78 g, 26.5 mmol), toluene-*p*-sulfonyl chloride (6.08 g, 31.8 mmol) and pyridine (43 cm^3) gave the crude product, which was purified by column chromatography on flash silica (eluent 1:3 ethyl acetate–light petroleum ether) to give (−)-(2*S*,3*S*)-3-(*tert*-butyldimethylsilyloxymethyl)oxiran-2-ylmethyl 4-methylbenzenesulfonate (8.58 g, 23.1 mmol, 87%) as a colourless oil; $[\alpha]_D^{24}$ −16.8 (*c* 1.19 in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 0.04 [6 H, s, Si(CH$_3$)$_2$], 0.86 [9 H, s, C(CH$_3$)$_3$], 2.45 (3 H, s, Ar-CH$_3$), 2.95–2.97 (1 H, m, 3-H), 3.14–3.17 (1 H, m, 2-H), 3.66 (1 H, dd, *J* 12.1, 4.0, one of CH$_2$OTBDMS), 3.83 (1 H, dd, *J* 12.1, 2.5, one of CH$_2$OTBDMS), 3.98 (1 H, dd, *J* 11.4, 6.0, one of CH$_2$OTs), 4.26 (1 H, dd, *J* 11.4, 3.6, one of CH$_2$OTs), 7.35 (2 H, d, *J* 8.2, Ar-H), 7.80 (2 H, d, *J* 8.4, Ar-H); δ_C(75 MHz; $CDCl_3$) −5.40 [2 C, Si(CH$_3$)$_2$], 18.29 (*C*Me$_3$), 21.66 (Ar-CH$_3$), 25.79 [3 C, C(*C*H$_3$)$_3$], 51.85 (3-C), 56.47 (2-C), 61.78, 69.73, 127.93, 129.87, 132.70, 145.01; ν_{max}(thin film)/cm^{-1} 2920 (s), 2845 (s), 1720 (w), 1590 (m), 1450 (m), 1350 (s), 1250 (m), 1170 (s), 1130 (m), 1100 (m), 1080 (m), 1030 (w), 1000 (w), 960 (s), 870 (m), 820 (s), 770 (s), 650 (m); *m/z* (EI) 371 (M$^+$ − 1, 8%), 355 (10), 329 (11), 315 (37), 297 (7), 285 (11), 271 (4), 255 (7), 229 (100), 165 (11), 155 (27), 143 (95), 129 (14), 117 (18), 101 (22), 91 (65), 75 (32), 59 (22), 41 (12) (Found: C, 55.1; H, 7.75; S, 8.55. Calc. for $C_{17}H_{28}O_5SSi$: C, 54.84; H, 7.53; S, 8.60%).

(−)-(2*S*,3*S*)-1-(*N*,*N*-Diallylamino)-4-*tert*-butyldimethylsilyloxy-2,3-epoxybutane (−)-10. A procedure similar to (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane using (−)-(2*S*,3*S*)-3-(*tert*-butyldimethylsilyloxymethyl)oxiran-2-ylmethyl 4-methylbenzenesulfonate (3.30 g, 8.87 mmol), potassium iodide (0.74 g, 4.43 mmol), diallylamine (1.72 g, 17.7 mmol, 2.19 ml) and DMF (29 cm^3) gave the crude product which was purified by column chromatography on flash silica (eluent 5:1 ethyl acetate–light petroleum) to give (2*S*,3*S*)-1-(*N*,*N*-diallylamino)-4-*tert*-butyldimethylsilyloxy-2,3-epoxybutane (1.84 g, 6.20 mmol, 70%) as a yellow oil; $[\alpha]_D^{20}$ −11.2° (*c* 1.22 in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 0.07 [6 H, s, Si(CH$_3$)$_2$], 0.89 [9 H, s, C(CH$_3$)$_3$], 2.52 (1 H, dd, *J* 13.6, 6.0, one of 1-CH$_2$), 2.72 (1 H, dd, *J* 13.6, 4.2, one of 1-CH$_2$), 2.85 (1 H, ddd, *J* 4.8, 3.6, 2.2, 3-H), 2.99 (1 H, ddd, *J* 6.0, 4.2, 2.2, 2-H), 3.12 (2 H, dd, *J* 14.0, 6.4, 2 × allylic C*H*H), 3.23 (2 H, dd, *J* 14.0, 6.4, 2 × allylic C*H*H), 3.69 (1 H, dd, *J* 11.4, 4.8, one of CH$_2$OTBDMS), 3.79 (1 H, dd, *J* 11.4, 3.6, one of CH$_2$OTBDMS), 5.13–5.22 (4 H, m, CH=C*H*$_2$ × 2), 5.79–5.92 (2 H, m, C*H*=CH$_2$ × 2); δ_C(75 MHz; $CDCl_3$) −5.36 [2 C, Si(CH$_3$)$_2$], 18.31 (*C*Me$_3$), 25.85 [3 C, C(*C*H$_3$)$_3$], 54.61 (2-C), 54.82, 57.10 (3-C), 57.27, 63.29, 117.67 (2 C, CH=*C*H$_2$ × 2), 135.31 (2 C, *C*H=CH$_2$ × 2); ν_{max}(thin film)/cm^{-1} 2950 (s), 2930 (s), 2900 (m), 2860 (s), 2800 (m), 1640 (w), 1470 (m), 1420 (w), 1360 (w), 1250 (s), 1180 (w), 1140 (m), 1100 (s), 1060 (w), 990 (w), 915 (m), 835 (s), 780 (m); *m/z* (EI) 297 (M$^+$, 3%), 282 (19), 270 (3), 256 (29), 240 (12), 233 (7), 158 (5), 152 (10), 117 (30), 110 (100), 96 (10), 89 (18), 73 (33), 59 (21), 41 (50) (Found: M$^+$, 297.213. Calc. for $C_{16}H_{31}NO_2Si$: *M*, 297.212).

Typical procedure for formation of 4-methylbenzenesulfonate esters

(±)-(2*S,3*S**)-3-Propyloxiran-2-ylmethyl 4-methylbenzenesulfonate.**[4] Toluene-*p*-sulfonyl chloride (18.6 g, 97.2 mmol) in pyridine (40 cm^3) was added to a solution of (±)-(2*S**,3*S**)-3-propyloxirane-2-methanol (9.40 g, 81.0 mmol) in pyridine (20 cm^3) under N_2 at −10 °C. The reaction mixture was stirred for 1 h then transferred to a fridge (−10 °C) and left for 24 h. The reaction mixture was poured into 1 M sulfuric acid (200 cm^3) and ice (100 g) and stirred vigorously for 10 min. The product was extracted with diethyl ether (4 × 50 cm^3), dried ($MgSO_4$), filtered and concentrated. Column chromatography on flash silica (eluent 10% ethyl acetate–90% light petroleum) gave (±)-(2*S**,3*S**)-3-propyloxiran-2-ylmethyl 4-methylbenzenesulfonate (16.0 g, 59.3 mmol, 73%) as a colourless oil: δ_H(300 MHz; $CDCl_3$) 0.92 (3 H, t, *J* 7.2, CH$_2$C*H*$_3$), 1.40–1.48 (4 H, m, CH$_2$CH$_2$), 2.44 (3 H, s, Ar-CH$_3$), 2.77–2.78 (1 H, m, 3-H), 2.94 (1 H, m, 2-H), 3.96 (1 H, dd, *J* 11.3, 5.7, one of CH$_2$OTs), 4.18 (1 H, dd, *J* 11.3, 3.6, remaining CH$_2$OTs), 7.35 (2 H, d, *J* 7.8, Ar-H), 7.79 (2 H, d, *J* 7.8, Ar-H); δ_C(75 MHz; $CDCl_3$) 12.76 (CH$_2$*C*H$_3$), 18.03 (*C*H$_2$CH$_3$), 20.60 (Ar-CH$_3$), 32.23 (*C*H$_2$CH$_2$CH$_3$), 53.44 (3-C), 55.49 (2-C), 69.22 (*C*H$_2$OTs), 126.85, 128.85, 131.64, 144.01; ν_{max}(thin film)/cm^{-1} 2950 (s), 2930 (s), 2870 (m), 1600 (m), 1450 (m), 1360 (s), 1190 (s), 1110 (m), 960 (m), 900 (w), 820 (m), 790 (m), 670 (s); *m/z* (EI) 270 (M$^+$, 13%), 227 (7), 155 (100), 99 (5), 91 (95), 65 (15), 55 (27), 43 (26) (Found: C, 57.95; H, 6.70; S, 11.90. Calc. for $C_{13}H_{18}O_4S$: C, 57.78; H, 6.67; S, 11.85%).

(−)-(2*S*,3*S*)-3-Propyloxiran-2-ylmethyl 4-methylbenzenesulfonate.[4] A similar procedure to (±)-(2*S**,3*S**)-3-propyloxiran-2-ylmethyl 4-methylbenzenesulfonate using toluene-*p*-sulfonyl chloride (16.5 g, 86.2 mmol) and (−)-(2*S*,3*S*)-3-propyloxirane-2-methanol (8.33 g, 71.8 mmol). Column chromatography on flash silica (eluent 10% ethyl acetate–90% light petroleum) gave (−)-(2*S*,3*S*)-3-propyloxiran-2-ylmethyl 4-methylbenzenesulfonate (17.3 g, 64.0 mmol, 89%) as colourless needles; mp 44–

45 °C; $[\alpha]_D^{20}$ −32.7 (*c* 1.09, in ethanol). Spectroscopic data are consistent with that of (±)-(2*S**,3*S**)-3-propyloxirane-2-ylmethyl 4-methylbenzenesulfonate.

(−)-(2*S*,3*R*)-3-Propyloxiran-2-ylmethyl 4-methylbenzenesulfonate.[4] A similar procedure to (±)-(2*S**,3*S**)-3-propyloxiran-2-ylmethyl 4-methylbenzenesulfonate using toluene-*p*-sulfonyl chloride (15.8 g, 82.6 mmol) and (−)-(2*S*,3*R*)-3-propyloxirane-2-methanol (7.98 g, 68.8 mmol). Column chromatography on flash silica (eluent 50% ethyl acetate–50% light petroleum) gave (−)-(2*S*,3*R*)-3-propyloxiran-2-ylmethyl 4-methylbenzenesulfonate (17.2 g, 63.7 mmol, 93%) as a colourless oil; $[\alpha]_D^{20}$ −13.3 (*c* 1.14, in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 0.93 (3 H, t, *J* 6.9, CH_3), 1.37–1.50 (4 H, m, CH_2CH_2), 2.46 (3 H, s, Ar-CH_3), 2.97–3.03 (1 H, m, 3-H), 3.13–3.19 (1 H, m, 2-H), 4.08 (1 H, dd, *J* 11.0, 6.4, one of CH_2OTs), 4.18 (1 H, dd, *J* 11.0, 4.6, remaining CH_2OTs), 7.37 (2 H, d, *J* 8.1, Ar-H), 7.82 (2 H, d, *J* 8.1, Ar-H); δ_C(75 MHz; $CDCl_3$) 13.82 (CH_3), 19.80 (CH_2CH_3), 21.65 (Ar-CH_3), 29.69 ($CH_2CH_2CH_3$), 52.94 (3-C), 56.42 (2-C), 68.09 (CH_2OTs), 127.93, 129.88, 132.65, 145.06; ν_{max}(thin film)/cm^{-1} 2950 (s), 2930 (s), 2870 (m), 1595 (s), 1495 (w), 1465 (m), 1450 (m), 1440 (w), 1390 (w), 1350 (s), 1300 (w), 1285 (w), 1210 (w), 1180 (s), 1170 (s), 1095 (s), 1015 (w), 950 (m), 910 (w), 810 (m), 780 (m), 660 (m); *m/z* (EI) 270 (M^+, 11%), 249 (11), 227 (11), 155 (100), 91 (87), 83 (7), 65 (20), 55 (25), 41 (15) (Found: C, 57.60; H, 6.60; S, 11.70. Calc. for $C_{13}H_{18}O_4S$: C, 57.78; H, 6.67; S, 11.85%).

Typical procedure for formation of 2,3-epoxy amines.

(±)-(2*S,3*S**)-1-(*N*,*N*-Dibenzylamino)-2,3-epoxyhexane (±)-8**

To a solution of (±)-(2*S**,3*S**)-3-propyloxiran-2-ylmethyl 4-methylbenzenesulfonate (3.63 g, 13.4 mmol) and potassium iodide (1.10 g, 6.59 mmol) in DMF (40 cm^3) under N_2, dibenzylamine (5.64 g, 28.6 mmol, 5.50 cm^3) was added. The reaction mixture was stirred for 3 days at room temperature. It was then washed with aqueous $NaHCO_3$ (100 cm^3) and water (200 cm^3). The aqueous solution was extracted with diethyl ether (4 × 50 cm^3). The extracts were dried ($MgSO_4$), filtered, concentrated and the product was purified by column chromatography on flash silica (eluent 10% ethyl acetate–90% light petroleum) to give (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (2.98 g, 10.1 mmol, 75%) as a yellow oil; δ_H(300 MHz; $CDCl_3$) 0.93 (3 H, t, *J* 6.6, CH_3), 1.36–1.44 (4 H, m, CH_2CH_2), 2.48 (1 H, dd, *J* 13.6, 6.0, one of CH_2NBn_2), 2.63–2.65 (1 H, m, 3-H), 2.69 (1 H, dd, *J* 13.6, 3.9, remaining CH_2NBn_2), 2.86–2.87 (1 H, m, 2-H), 3.55 (2 H, d, *J* 13.5, 2 × C*H*HPh), 3.77 (2 H, d, *J* 13.5, 2 × C*H*HPh), 7.24–7.40 (10 H, m, Ar-H); δ_C(75 MHz, $CDCl_3$) 13.94 (CH_3), 19.28 (CH_2CH_3), 33.84 ($CH_2CH_2CH_3$), 55.51, 56.81 (3-C), 57.21 (2-C), 58.87, 126.89, 128.19, 128.74, 139.36; ν_{max}(thin film)/cm^{-1} 2965 (s), 2940 (s), 2880 (m), 2805 (m), 1600 (w), 1500 (m), 1460 (s), 1380 (m), 1250 (w), 1135 (w), 1085 (w), 1040 (w), 980 (w), 910 (m), 850 (w), 750 (s), 705 (m); *m/z* (EI) 295 (M^+, 48%), 252 (21), 222 (9), 210 (73), 204 (14), 181 (9), 118 (7), 106 (10), 91 (100), 65 (15), 41 (8) (Found: C, 81.35; H, 8.40; N, 4.60. Calc. for $C_{20}H_{25}NO$: C, 81.36; H, 8.47; N, 4.75%).

(±)-(2*S,3*S**)-1-(*N*,*N*-Diallylamino)-2,3-epoxyhexane (±)-9.** A similar procedure to (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (±)-**8** using (±)-(2*S**,3*S**)-3-propyloxiran-2-ylmethyl 4-methylbenzenesulfonate (3.35 g, 12.4 mmol), potassium iodide (1.50 g, 8.98 mmol) and diallylamine (2.65 g, 27.3 mmol, 3.37 cm^3); purified by column chromatography on flash silica (eluent 20% ethyl acetate–80% light petroleum) to give (±)-(2*S**,3*S**)-1-(*N*,*N*-diallylamino)-2,3-epoxyhexane (2.00 g, 10.3 mmol, 83%) as a yellow oil; δ_H(300 MHz; $CDCl_3$) 0.96 (3 H, t, *J* 7.2, CH_3), 1.42–1.57 (4 H, m, CH_2CH_2), 2.47 [1 H, dd, *J* 13.6, 6.3, one of $CH_2N(allyl)_2$], 2.70 [2 H, apparent dd, *J* 13.6, 3.5, remaining $CH_2N(allyl)_2$ and 3-H], 2.82–2.85 (1 H, m, 2-H), 3.11 (2 H, dd, *J* 13.8, 6.3, 2 × allylic C*H*H), 3.23 (2 H, dd, *J* 13.8, 6.3, 2 × allylic C*H*H), 5.14–5.22 (4 H, m, CH=CH_2 × 2), 5.79–5.92 (2 H, m, C*H*=CH_2 × 2); δ_C(75 MHz; $CDCl_3$) 14.96 (CH_3), 19.30 (CH_2CH_3), 33.89 ($CH_2CH_2CH_3$), 55.30, 57.01, 57.31, 117.68 (2 C, CH=CH_2 × 2), 135.35 (2 C, CH=CH_2 × 2); ν_{max}(thin film)/cm^{-1} 3100 (s), 2965 (s), 2930 (s), 2900 (m), 2870 (m), 2805 (m), 1640 (m), 1460 (s), 1430 (s), 1390 (w), 1375 (w), 1360 (w), 1340 (w), 1260 (m), 1160 (m), 1050 (m), 925 (s), 850 (w); *m/z* (EI) 195 (M^+, 35%), 180 (24), 168 (32), 154 (22), 110 (100), 96 (6), 81 (11), 68 (12), 55 (11), 41 (42) (Found: M^+, 195.163. Calc. for $C_{12}H_{21}NO$: *M*, 195.162).

(−)-(2*S*,3*S*)-1-(*N*,*N*-Dibenzylamino)–2,3-epoxyhexane (−)-8. A similar procedure to (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (±)-**8** using (−)-(2*S*,3*S*)-3-propyloxiran-2-ylmethyl 4-methylbenzenesulfonate (5.26 g, 19.5 mmol), potassium iodide (1.63 g, 9.74 mmol) and dibenzylamine (7.68 g, 39.0 mmol, 7.48 cm^3); purified by column chromatography on flash silica (eluent 10% ethyl acetate–90% light petroleum) to give (−)-(2*S*,3*S*)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (4.60 g, 15.6 mmol, 80%) as a yellow oil; $[\alpha]_D^{20}$ −3.6 (*c* 1.56, in ethanol). Spectroscopic data are consistent with that of (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane.

(−)-(2*S*,3*S*)-1-(*N*,*N*-Diallylamino)-2,3-epoxyhexane (−)-9. A similar procedure to (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (±)-**8** using (−)-(2*S*,3*S*)-3-propyloxiran-2-ylmethyl 4-methylbenzenesulfonate (5.00 g, 18.5 mmol), potassium iodide (1.54 g, 9.25 mmol) and diallylamine (3.60 g, 37.0 mmol, 4.60 cm^3); purified by column chromatography on flash silica (eluent 20% ethyl acetate–80% light petroleum) to give (−)-(2*S*,3*S*)-1-(*N*,*N*-diallylamino)-2,3-epoxyhexane (3.33 g, 17.1 mmol, 92%) as a yellow oil; $[\alpha]_D^{20}$ −28.6 (*c* 1.02, in ethanol). Spectroscopic data are consistent with that of (±)-(2*S**,3*S**)-1-(*N*,*N*-diallylamino)-2,3-epoxyhexane.

(+)-(2*S*,3*R*)-1-(*N*,*N*-Dibenzylamino)-2,3-epoxyhexane (+)-11. A similar procedure to (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (±)-**8** using (−)-(2*S*,3*R*)-3-propyloxiran-2-ylmethyl 4-methylbenzenesulfonate (5.06 g, 18.7 mmol), potassium iodide (1.56 g, 9.35 mmol) and dibenzylamine (7.38 g, 37.5 mmol, 7.20 cm^3); purified by column chromatography on flash silica (eluent 10% ethyl acetate–90% light petroleum) to give (+)-(2*S*,3*R*)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (4.62 g, 15.7 mmol, 84%) as a yellow oil; $[\alpha]_D^{20}$ +27.8 (*c* 1.18, in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 0.92 (3 H, t, *J* 6.3, CH_3), 1.33–1.47 (4 H, m, CH_2CH_2), 2.46 (1 H, dd, *J* 13.8, 6.6, one of 1-CH_2), 2.77 (1 H, dd, *J* 13.8, 3.3, remaining 1-CH_2), 2.88 (1 H, dt, *J* 3.9, 6.6, 3-H), 3.13 (1 H, ddd, *J* 6.6, 3.9, 3.3, 2-H), 3.51 (2 H, d, *J* 13.8, 2 × C*H*HPh), 3.83 (2 H, d, *J* 13.8, 2 × C*H*HPh), 7.21–7.40 (10 H, m, Ar-H); δ_C(75 MHz, $CDCl_3$) 13.96 (CH_3), 20.03 (CH_2CH_3), 30.09 ($CH_2CH_2CH_3$), 51.90, 55.74 (2-C or 3-C), 55.82 (2-C or 3-C), 58.75, 126.91, 128.19, 128.83, 139.33; ν_{max}-(thin film)/cm^{-1} 2960 (s), 2920 (m), 2885 (m), 2840 (m), 2800 (s), 1600 (w), 1500 (m), 1460 (s), 1380 (m), 1330 (w), 1250 (m), 1130 (m), 1080 (m), 1040 (w), 980 (w), 910 (w), 850 (w), 750 (s), 710 (m); *m/z* (EI) 295 (M^+, 1%), 287 (8), 277 (19), 262 (9), 252 (25), 236 (26), 210 (53), 106 (6), 91 (100), 65 (9), 55 (6) (Found: C, 81.40; H, 8.45; N, 4.80. Calc. for $C_{20}H_{25}NO$: C, 81.36; H, 8.47; N, 4.75%).

(−)-(2*S*,3*R*)-1-(*N*,*N*-Diallylamino)-2,3-epoxyhexane (−)-12. A similar procedure to (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (±)-**8** using (−)-(2*S*,3*R*)-3-propyloxiran-2-ylmethyl 4-methylbenzenesulfonate (5.00 g, 18.5 mmol), potassium iodide (1.54 g, 9.25 mmol) and diallylamine (3.60 g, 37.0 mmol, 4.60 cm^3); purified by column chromatography on flash silica (eluent 20% ethyl acetate–80% light petroleum) to give (−)-(2*S*,3*R*)-1-(*N*,*N*-diallylamino)-2,3-epoxyhexane (3.00 g, 15.4 mmol, 83%) as a yellow oil; $[\alpha]_D^{20}$ −15.2 (*c* 1.26, in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 0.98 (3 H, t, *J* 6.9, CH_3), 1.42–1.60 (4 H, m, CH_2CH_2), 2.44 (1 H, dd, *J* 13.6, 6.3, one of 1-CH_2), 2.79 (1 H, dd, *J* 13.6, 3.6, remaining 1-CH_2), 2.92 (1 H, dt, *J* 9.9, 5.4, 3-H), 3.05–3.16 (3 H, m, 2 × allylic C*H*H, 2-H), 3.27 (2 H, dd, *J* 14.1, 6.0, 2 × allylic C*H*H), 5.14–5.23 (4 H, m, CH=CH_2 × 2), 5.80–5.94 (2 H, m, C*H*=CH_2 × 2); δ_C(75 MHz; $CDCl_3$) 14.00 (CH_3), 20.05 (CH_2CH_3), 30.14 ($CH_2CH_2CH_3$), 51.81, 55.52 (C-2 or C-3), 55.98 (C-2 or C-3), 57.27, 117.79 (2 C, CH=CH_2 × 2),

135.37 (2 C, *C*H=CH_2 × 2); ν_{max}(thin film)/cm^{-1} 2970 (s), 2940 (m), 2900 (m), 2810 (m), 2800 (m), 1640 (m), 1460 (s), 1430 (m), 1365 (w), 1265 (m), 1170 (w), 1155 (w), 1125 (w), 1095 (w), 1010 (m), 920 (s), 850 (m), 770 (w), 680 (w); *m/z* (EI) 196 (M^+ + 1, 6%), 155 (18), 142 (6), 124 (11), 110 (82), 96 (22), 91 (37), 82 (8), 77 (15), 70 (29), 55 (24), 41 (100) [Found: (M^+ − H) 194.154. Calc. for $C_{12}H_{20}NO$: *M*, 194.154].

(±)-*N*-[(2*S,3*S**)-2,3-Epoxyhexyl]piperidine (±)-7.** A similar procedure to (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (±)-**8** using (±)-(2*S**,3*S**)-3-propyloxirane-2-ylmethyl 4-methylbenzenesulfonate (4.10 g, 15.2 mmol), potassium iodide (1.27 g, 7.60 mmol) and piperidine (2.58 g, 3.00 cm^3, 30.4 mmol); purified by column chromatography on flash silica (eluent 67% ethyl acetate–33% light petroleum) to give (±)-*N*-[(2*S**,3*S**)-2,3-epoxyhexyl]piperidine (2.10 g, 11.5 mmol, 76%) as a yellow oil; δ_H(300 MHz; $CDCl_3$) 0.96 (3 H, t, *J* 7.2, CH_3), 1.42–1.64 (10 H, m, CH_2CH_2CH_3, piperidine 3-CH_2, 4-CH_2, 5-CH_2), 2.33 (1 H, dd, *J* 13.0, 6.6, one of 1′-CH_2), 2.44–2.51 (4 H, m, piperidine 2-CH_2, 6-CH_2), 2.62 (1 H, dd, *J* 13.0, 3.6, remaining 1′-CH_2), 2.66–2.68 (1 H, m, 3′-H), 2.87–2.88 (1 H, m, 2′-H); δ_C(75 MHz; $CDCl_3$) 13.90 (CH_3), 19.24 (*C*H_2CH_3), 24.09, 25.86, 33.80 (*C*H_2CH_2CH_3), 54.91, 56.60 (C-2′ or C-3′), 56.78 (C-2′ or C-3′), 61.32; ν_{max}(thin film)/cm^{-1} 2940 (s), 2920 (s), 2860 (m), 2800 (m), 1650 (w), 1640 (w), 1625 (w), 1475 (m), 1465 (s), 1455 (m), 1390 (w), 1360 (w), 1330 (w), 1305 (m), 1275 (w), 1250 (w), 1160 (m), 1130 (s), 1050 (w), 1000 (w), 970 (w), 910 (m), 860 (w), 780 (w); *m/z* (EI) 183 (M^+, 12%), 140 (14), 112 (6), 98 (100), 85 (30), 70 (13), 55 (28), 41 (28) (Found: C, 71.90; H, 11.55; N, 7.35. Calc. for $C_{11}H_{21}NO$: C, 72.13; H, 11.48; N, 7.65%).

TMSOTf mediated aziridinium salt formation (Scheme 3)

(±)-(2*R,1′*S**)-1,1-Dibenzyl-2-(1′-trimethylsilyloxybutyl)-aziridinium trifluoromethanesulfonate (±)-13**

Trimethylsilyl trifluoromethanesulfonate (0.29 g, 0.25 cm^3, 1.29 mmol) was added to a solution of (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (0.38 g, 1.29 mmol) in $CDCl_3$ (6 cm^3) at −42 °C under nitrogen. After 10 min, the mixture was allowed to warm to room temperature. The ^{1}H NMR spectrum of the resulting solution was then taken; δ_H(300 MHz; $CDCl_3$) 0.11 [9 H, s, Si$(CH_3)_3$], 0.92 (3 H, t, *J* 9.0, CH_3), 1.23–1.44 (2 H, m, CH_2CH_3), 1.69–1.80 (2 H, m, CH_2CH_2CH_3), 3.23 (1 H, dd, *J* 8.0, 2.7, one of aziridinium CH_2), 3.32 (1 H, dd, *J* 8.0, 2.7, one of aziridinium CH_2), 3.65 (1 H, t, *J* 8.0, aziridinium CH), 4.27 (1 H, d, *J* 13.6, C*H*HPh), 4.43 (1 H, d, *J* 13.6, C*H*HPh), 4.60 (2 H, d, *J* 13.6, 2 × C*H*HPh), 4.70 (1 H, dd, *J* 3.5, 2.8, CHO), 7.30–7.53 (10 H, m, Ar-H).

(±)-(2*R,1′*S**)-1,1-Diallyl-2-(1′-trimethylsilyloxybutyl)-aziridinium trifluoromethanesulfonate (±)-14**

Trimethylsilyl trifluoromethanesulfonate (0.08 g, 0.07 cm^3, 0.35 mmol) was added to a solution of (±)-(2*S**,3*S**)-1-(*N*,*N*-diallylamino)-2,3-epoxyhexane (0.07 g, 0.35 mmol) in $CDCl_3$ (2 cm^3) at −42 °C under nitrogen. After 10 min, the mixture was allowed to warm to room temperature. The ^{1}H NMR spectrum of the resulting solution was then taken; δ_H(300 MHz; $CDCl_3$) 0.13 [9 H, s, Si$(CH_3)_3$], 0.91 (3 H, t, *J* 7.2, CH_2CH_3), 1.30–1.48 (2 H, m, CH_2CH_3), 1.67–1.80 (2 H, m, CH_2CH_2CH_3), 3.05 (1 H, dd, *J* 8.0, 3.0, one of aziridinium CH_2), 3.37 (1 H, dd, *J* 8.0, 3.0, one of aziridinium CH_2), 3.61 (1 H, t, *J* 8.0, aziridinium CH), 3.81–3.97 (4 H, m, 4 × allylic C*H*H), 4.56 (1 H, t, *J* 4.2, CHO), 5.46–5.60 (4 H, m, CH=CH_2 × 2), 5.85–5.98 (2 H, m, C*H*=CH_2 × 2).

(±)-(1*R,1′*S**)-1-(1′-Trimethylsilyloxybutyl)-3-azoniaspiro-[5.2]octane trifluoromethanesulfonate (±)-15.**

Trimethylsilyl trifluoromethanesulfonate (0.24 g, 0.21 cm^3, 1.09 mmol) was added to a solution of (±)-*N*-[(2′*S**,3′*S**)-2′,3′-epoxyhexyl]piperidine (0.20 g, 1.09 mmol) in $CDCl_3$ (3 cm^3) at −42 °C under nitrogen. After 10 min, the mixture was allowed to warm to room temperature. The ^{1}H NMR spectrum of the resulting solution was then taken (before doing this, the NMR tube was flushed with nitrogen); δ_H(400 MHz; $CDCl_3$) 0.09 [9 H, s, Si$(CH_3)_3$], 0.89 (3 H, t, *J* 7.3, CH_2CH_3), 1.26–1.47 (3 H, m, CH_2CH_3, one of CH_2CH_2CH_3), 1.64–1.85 (7 H, m, one of CH_2CH_2CH_3, and piperidine 5-CH_2, 6-CH_2, 7-CH_2), 2.89 (1 H, dd, *J* 7.2, 2.9, one of 2-CH_2), 3.11–3.14 (2 H, m, one of 2-CH_2, and one of 4-CH_2 or one of 8-CH_2), 3.26–3.33 (2 H, m, 1-CH, and one of 4-CH_2 or one of 8-CH_2), 3.43–3.49 (2 H, one of 4-CH_2, one of 8-CH_2), 4.54 (1 H, t, *J* 4.6, CHO).

Table 1 entries

Typical procedure. (±)-1-[(2′*R,3′*S**)-2′-(*N*,*N*-Dibenzylamino)-3′-hydroxyhexyl]-2-pyridone (entry 1)**

Trimethylsilyl trifluoromethanesulfonate (0.27 g, 0.24 cm^3, 1.22 mmol) was added to a solution of (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (0.30 g, 1.02 mmol) in dichloromethane (6 cm^3) at −78 °C under nitrogen. After 10 min, 2-trimethylsilyloxypyridine (0.34 g, 2.04 mmol) was added to the solution which was then allowed to warm to room temperature and stirred for 120 h. Methanol (9 cm^3) and potassium carbonate (0.80 g) were added and the mixture stirred for a further 12 h. Solvent was then removed *in vacuo* and the residue was purified by column chromatography on flash silica (eluent 85% ethyl acetate–15% light petroleum) to give (±)-1-[(2′*R**,3′*S**)-2′-(*N*,*N*-dibenzylamino)-3′-hydroxyhexyl]-2-pyridone (0.37 g, 0.95 mmol, 93%) as a colourless viscous oil; δ_H(300 MHz; $CDCl_3$) 0.88 (3 H, t, *J* 6.9, CH_3), 1.25–1.44 (4 H, m, CH_2CH_2), 2.91–2.92 (1 H, m, C*H*NBn_2), 3.16 (1 H, d, *J* 6.9, OH), 3.68 (2 H, d, *J* 14.1, 2 × C*H*HPh), 3.80 (1 H, dd, *J* 13.5, 6.3, one of 1′-CH_2), 3.93 (2 H, d, *J* 14.1, 2 × C*H*HPh), 4.03–4.06 (1 H, m, *CH*OH), 4.59 (1 H, dd, *J* 13.5, 5.7, remaining 1′-CH_2), 6.21 (1 H, t, *J* 6.6, pyridone 5-H), 6.51 (1 H, d, *J* 9.0, pyridone 3-H), 7.21–7.38 (12 H, m, Ar-H and pyridone 4-H, 6-H); δ_C(75 MHz; $CDCl_3$) 14.02 (CH_3), 19.18 (*C*H_2CH_3), 38.46 (*C*H_2CH_2CH_3), 47.65, 54.56, 61.19 (*C*HNBn_2), 69.79 (CHOH), 106.26, 120.84, 127.00, 128.33, 128.38, 138.78, 139.55, 163.14; ν_{max}(thin film)/cm^{-1} 3480–3180 (br, s), 2940 (s), 2900 (m), 2880 (m), 1650 (s), 1570 (s), 1540 (m), 1490 (w), 1450 (m), 1360 (w), 1245 (m), 1170 (w), 1140 (m), 1100 (w), 1065 (s), 1025 (w), 970 (w), 840 (m), 750 (s), 700 (m); *m/z* (EI) 391 (M^+ + 1, 30%), 372 (6), 347 (10), 329 (71), 317 (100), 299 (42), 282 (18), 264 (6), 223 (6), 132 (5), 91 (37), 81 (17), 65 (26) (Found: C, 77.05; H, 7.90; N, 7.00. Calc. for $C_{25}H_{30}N_2O_2$: C, 76.92; H, 7.69; N, 7.18%).

A similar procedure was used for the following entries.

(±)-1-[(2′*R,3′*S**)-2′-(*N*,*N*-Diallylamino)-3′-hydroxyhexyl]-2-pyridone (entry 2).** From trimethylsilyl trifluoromethanesulfonate (0.41 g, 0.36 cm^3, 1.85 mmol), (±)-(2*S**,3*S**)-1-(*N*,*N*-diallylamino)-2,3-epoxyhexane (0.30 g, 1.54 mmol) and 2-trimethylsilyloxypyridine (0.51 g, 3.08 mmol); purified by column chromatography on flash silica (eluent 60% ethyl acetate–40% light petroleum) to give (±)-1-[(2′*R**,3′*S**)-2′-(*N*,*N*-diallylamino)-3′-hydroxyhexyl]-2-pyridone (0.37 g, 1.28 mmol, 83%) as a colourless viscous oil; δ_H(300 MHz; $CDCl_3$) 0.92 (3 H, t, *J* 6.3, CH_3), 1.30–1.58 (4 H, m, CH_2CH_2), 2.98 [1 H, dt, *J* 10.5, 5.1, CHN(allyl)$_2$], 3.13 (2 H, dd, *J* 14.7, 6.0, 2 × allylic C*H*H), 3.29 (2 H, dd, *J* 14.7, 6.0, 2 × allylic C*H*H), 3.75 (1 H, dd, *J* 13.8, 6.6, one of 1′-CH_2), 3.80–3.82 (1 H, m, C*H*OH), 4.44 (1 H, dd, *J* 13.8, 5.1, remaining 1′-CH_2), 5.01–5.13 (4 H, m, CH=CH_2 × 2), 5.58–5.71 (2 H, m, C*H*=CH_2 × 2), 6.20 (1 H, t, *J* 6.6, pyridone 5-H), 6.57 (1 H, d, *J* 8.7, pyridone 3-H), 7.32–7.39 (2 H, m, pyridone 4-H, 6-H); δ_C(75 MHz, $CDCl_3$) 14.04 (CH_3), 19.14 (*C*H_2CH_3), 38.21 (*C*H_2CH_2CH_3), 48.13, 53.45, 62.24 [*C*HN(allyl)$_2$], 70.35 (CHOH), 105.85, 116.78 (2 C, CH=*C*H_2 × 2), 120.42, 136.71 (2 C, *C*H=CH_2 × 2), 139.14, 139.60, 163.20; ν_{max}(thin film)/cm^{-1} 3500–3220 (br, s), 2950 (s), 2920 (s), 2890 (m), 1650 (s), 1570 (s), 1540 (m), 1460 (m), 1445 (m), 1425 (m), 1350 (w), 1330 (w), 1250 (w), 1145 (m), 910 (m), 840 (m), 765 (s); *m/z* (El) 291 (M^+ + 1, 20%), 249 (13), 237 (7), 224 (27),

217 (100), 195 (12), 182 (48), 164 (14), 152 (14), 140 (16), 122 (53), 108 (18), 96 (79), 81 (62), 67 (30), 55 (41), 41 (59) (Found: M^+, 290.200. Calc. for $C_{17}H_{28}N_2O_2$: *M*, 290.199).

(+)-1-[(2′*R*,3′*R*)-2′-(*N*,*N*-Diallylamino)-3′-hydroxy-4′-*tert*-butyldimethylsilyloxybutyl]-2-pyridone (entry 3). From trimethylsilyl trifluoromethanesulfonate (0.22 g, 0.19 cm^3, 0.98 mmol), (2*S*,3*S*)-1-(*N*,*N*-diallylamino)-4-*tert*-butyldimethylsilyloxy-2,3-epoxybutane (0.29 g, 0.98 mmol) and 2-trimethylsilyloxypyridine (0.33 g, 1.95 mmol); purified by column chromatography on flash silica (eluent 50% ethyl acetate–50% light petroleum) to give (+)-1-[(2′*R*,3′*R*)-2′-(*N*,*N*-diallylamino)-3′-hydroxy-4′-*tert*-butyldimethylsilyloxybutyl]-2-pyridone (0.30 g, 0.77 mmol, 79%) as a viscous yellow oil; $[\alpha]_D^{20}$ +132.90 (*c* 1.24 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 0.05 [6 H, s, $Si(CH_3)_2$], 0.87 [9 H, s, $C(CH_3)_3$], 3.00–3.06 [3 H, m, 2 × allylic C*H*H, C*H*N(allyl)$_2$], 3.33 (2 H, dd, *J* 14.8, 5.4, 2 × allylic C*H*H), 3.55 (1 H, dd, *J* 10.1, 4.6, one of CH_2OTBDMS), 3.62 (1 H, dd, *J* 10.1, 8.4, one of CH_2O-TBDMS), 3.74 (1 H, dd, *J* 13.5, 8.4, one of 1′-CH_2), 3.89 (1 H, dt, *J* 3.5, 8.4 *CH*OH), 4.30 (1 H, dd, *J* 13.5, 4.0, one of 1′-CH_2), 4.97–5.05 (4 H, m, CH=CH_2 × 2), 5.51–5.61 (2 H, m, C*H*=CH_2 × 2), 6.10 (1 H, t, *J* 6.7, pyridone 5-H), 6.49 (1 H, d, *J* 8.8, pyridone 3-H), 7.28–7.31 (2 H, m, pyridone 4-H, 6-H); δ_C(75 MHz; $CDCl_3$) −5.40 [2 C, $Si(CH_3)_2$], 18.19 (*C*Me_3), 25.84 [3 C, C(*C*H_3)$_3$], 47.79, 53.08, 58.35 [*C*HN(allyl)$_2$], 65.30, 70.00 (CHOH), 104.98, 116.62 (2 C, CH=*C*H_2 × 2), 120.15, 136.46 (2 C, *C*H=CH_2 × 2), 139.32, 139.49, 162.72 (C=O); ν_{max}(thin film)/cm^{-1} 3550–3150 (br, s), 2950 (s), 2880 (s), 2840 (s), 1730 (w), 1650 (s), 1580 (s), 1560 (s), 1550 (s), 1460 (s), 1410 (m), 1390 (m), 1350 (m), 1340 (m), 1250 (s), 1130 (s), 1000 (s), 1050 (s), 980 (m), 920 (s), 830 (s), 760 (s), 720 (m), 660 (m); *m/z* (EI) 393 (M^+ + 1, 18%), 377 (8), 351 (67), 335 (25), 297 (18), 284 (75), 266 (10), 254 (6), 238 (12), 217 (100), 175 (8), 152 (62), 143 (17), 122 (60), 110 (46), 96 (68), 81 (47), 73 (90) (Found: C, 64.35; H, 9.00; N, 7.20. Calc. for $C_{21}H_{36}N_2O_3Si$: C, 64.29; H, 9.18; N, 7.14%).

(±)-1-[(2′*R,3′*S**)-2′-(*N*,*N*-Dibenzylamino)-3′-hydroxyhexyl]uracil (entry 4).** From trimethylsilyl trifluoromethanesulfonate (0.27 g, 0.24 cm^3, 1.22 mmol), (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (0.30 g, 1.02 mmol) and bis-*O*-trimethylsilyluracil (0.52 g, 2.04 mmol); purified by column chromatography on flash silica (eluent 67% ethyl acetate–33% light petroleum) to give (±)-1-[(2′*R**,3′*S**)-2′-(*N*,*N*-dibenzylamino)-3′-hydroxyhexyl]uracil (0.37 g, 0.91 mmol, 89%) as a white solid: mp 295–296 °C; δ_H(300 MHz; $CDCl_3$) 0.97 (3 H, t, *J* 7.2, CH_3), 1.25–1.60 (4 H, m, CH_2CH_2), 2.89–2.92 (1 H, m, $CHNBn_2$), 3.51 (2 H, d, *J* 14.1, 2 × C*H*HPh), 3.67 (1 H, dd, *J* 14.4, 9.3, one of 1′-CH_2), 4.00–4.05 (3 H, m, 2 × C*H*HPh and remaining 1′-CH_2), 4.16–4.18 (1 H, m, C*H*OH), 5.68 (1 H, d, *J* 7.8, uracil 5-H), 7.12 (1 H, d, *J* 7.8, uracil 6-H), 7.21–7.33 (10 H, m, Ar-H), 8.22 (1 H, br, NH); δ_C(75 MHz; $CDCl_3$) 13.97 (CH_3), 19.03 (CH_2CH_3), 38.70 ($CH_2CH_2CH_3$), 46.67, 54.34, 59.73, (*C*HNBn$_2$), 68.62 (CHOH), 100.65, 127.22, 128.39, 128.46, 139.11, 146.44, 150.26, 163.47; ν_{max}(thin film)/cm^{-1} 3460–3280 (br, s), 2900 (s), 2840 (m), 1650 (s), 1430 (m), 1400 (w), 1370 (w), 1340 (m), 1240 (w), 1170 (w), 1120 (w), 1070 (w), 1050 (m), 1010 (w), 960 (m), 730 (m), 680 (m); *m/z* (EI) 407 (M^+, 2%), 334 (74), 282 (43), 264 (13), 223 (9), 181 (11), 132 (18), 82 (8), 65 (14), 43 (7) (Found: C, 70.45; H, 7.00; N, 10.35. Calc. for $C_{24}H_{29}N_3O_3$: C, 70.76; H, 7.13; N, 10.32%).

(±)-1-[(2′*R,3′*S**)-2′-(*N*,*N*-Diallylamino)-3′-hydroxyhexyl]uracil (entry 5).** From trimethylsilyl trifluoromethanesulfonate (0.41 g, 0.36 cm^3, 1.85 mmol), (±)-(2*S**,3*S**)-1-(*N*,*N*-diallylamino)-2,3-epoxyhexane (0.30 g, 1.54 mmol) and bis-*O*-trimethylsilyluracil (0.79 g, 3.08 mmol); purified by column chromatography on flash silica (eluent 67% ethyl acetate–33% light petroleum) to give (±)-1-[(2′*R**,3′*S**)-2′-(*N*,*N*-diallylamino)-3′-hydroxyhexyl]uracil (0.43 g, 1.40 mmol, 91%) as a colourless viscous oil; δ_H(300 MHz; $CDCl_3$) 0.96 (3 H, t, *J* 7.2, CH_3), 1.31–1.62 (4 H, m, CH_2CH_2), 1.94 (1 H, br, OH), 2.90–2.94 [1 H, m, C*H*N(allyl)$_2$], 3.02 (2 H, dd, *J* 14.5, 7.2, 2 × allylic C*H*H), 3.42 (2 H, dd, *J* 14.5, 4.8, 2 × allylic C*H*H), 3.56 (1 H, dd, *J* 14.1, 9.0, one of 1′-CH_2), 3.89–3.90 (1 H, m, *CH*OH), 4.13 (1 H, dd, *J* 14.1, 3.3, remaining 1′-CH_2), 5.07–5.15 (4 H, m, CH=CH_2 × 2), 5.58–5.71 (3 H, m, C*H*=CH_2 × 2 and uracil 5-H), 7.20 (1 H, d, *J* 7.8, uracil 6-H), 9.08 (1 H, br, NH); δ_C(75 MHz; $CDCl_3$) 13.94 (CH_3), 18.98 (CH_2CH_3), 38.47 ($CH_2CH_2CH_3$), 46.59, 53.05, 61.15 [*C*HN(allyl)$_2$], 69.62 (CHOH), 100.54, 117.17 (2 C, CH=*C*H_2 × 2), 136.27 (2 C, *C*H=CH_2 × 2), 146.63, 150.91, 163.92; ν_{max}(thin film)/cm^{-1} 3500–3280 (br, s), 2940 (s), 2910 (s), 2860 (m), 1690 (s), 1650 (s), 1450 (s), 1430 (m), 1410 (m), 1365 (m), 1340 (m), 1240 (s), 1150 (w), 1130 (w), 1110 (w), 1085 (w), 1050 (w), 990 (w), 910 (m), 840 (m), 810 (m), 760 (s); *m/z* (EI) 307 (M^+, 7%), 280 (11), 266 (24), 234 (100), 193 (24), 182 (93), 164 (6), 150 (7), 140 (29), 122 (21), 110 (82), 96 (21), 82 (46), 70 (30), 55 (40), 41 (94) (Found: C, 62.70; H, 8.30; N, 13.75. Calc. for $C_{16}H_{25}N_3O_3$: C, 62.54; H, 8.14; N, 13.68%).

(±)-1-[(2′*R,3′*S**)-2′-Piperidino-3′-hydroxyhexyl]uracil (entry 6).** From trimethylsilyl trifluoromethanesulfonate (0.52 g, 0.46 cm^3, 2.36 mmol), (±)-*N*-[(2′*S**,3′*S**)-2′,3′-epoxyhexyl]-piperidine (0.36 g, 1.97 mmol) and bis-*O*-trimethylsilyluracil (1.01 g, 3.93 mmol). After usual work-up, tetrabutylammonium fluoride (20 cm^3, 1.0 M solution in tetrahydrofuran) was added and the mixture stirred for a further 100 min. Solvent was then removed *in vacuo* and the residue was purified by column chromatography on flash silica (eluent 50% ethyl acetate–50% acetone) to give (±)-1-[(2′*R**,3′*S**)-2′-piperidino-3′-hydroxyhexyl]uracil (0.46 g, 1.56 mmol, 79%) as a pale yellow solid; mp 135.3–136.5 °C; δ_H(300 MHz; [$^2H_6$]acetone) 0.91 (3 H, t, *J* 7.2, CH_3), 1.29–1.59 (10 H, m, CH_2CH_2CH$_3$, piperidine 3-CH_2, 4-CH_2, 5-CH_2), 2.37–2.52 (2 H, m, one of 2-CH_2, piperidine 6-CH_2), 2.69 (1 H, br, 2′-H), 2.83 (2 H, br, piperidine 2-C*H*H, 6-C*H*H), 3.78 (1 H, br, one of 1′-CH_2), 3.90 (1 H, br, C*H*OH), 4.03 (1 H, dd, *J* 13.5, 2.7, one of 1′-CH_2), 5.49 (1 H, d, *J* 7.8, uracil 5-H), 7.49 (1 H, d, *J* 7.8, uracil 6-H), 9.93 (1 H, br, NH); δ_C(75 MHz; [$^2H_6$]acetone) 14.41 (CH_3), 19.63 (CH_2CH_3), 25.64, 27.57, 39.54 ($CH_2CH_2CH_3$), 46.13, 51.44, 68.78, 68.82 (CHOH), 100.40, 147.91, 152.12, 164.30; ν_{max}(acetone)/cm^{-1} 3600–3400 (br, s), 2960 (s), 2930 (s), 1785 (w), 1770 (w), 1620 (s), 1415 (s), 1350 (s), 1200 (m), 1070 (m), 895 (m), 695 (w); *m/z* (EI) 296 (M^+ + 1, 16%), 278 (7), 242 (100), 222 (80), 184 (13), 170 (59), 152 (39), 142 (67), 124 (7), 111 (14), 100 (25), 84 (17), 69 (20), 55 (24), 41 (46) (Found: M^+, 295.189. Calc. for $C_{15}H_{25}N_3O_3$: *M*, 295.189).

(±)-1-[(2′*R,3′*S**)-2′-(*N*,*N*-Dibenzylamino)-3′-hydroxyhexyl]piperidine (entry 7).** From trimethylsilyl trifluoromethanesulfonate (0.27 g, 0.24 cm^3, 1.22 mmol), (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (0.30 g, 1.02 mmol) and piperidine (0.17 g, 0.20 ml, 2.04 mmol); purified by column chromatography on flash silica (eluent 67% ethyl acetate–33% light petroleum) to give (±)-*N*-[(2′*R**,3′*S**)-2′-(*N*,*N*-dibenzylamino)-3′-hydroxyhexyl]piperidine (0.23 g, 0.61 mmol, 60%) as a yellow oil; δ_H(400 MHz; $CDCl_3$) 0.95 (3 H, t, *J* 7.2, CH_3), 1.21–1.57 (10 H, m, CH_2CH_2CH$_3$, piperidine 3-CH_2, 4-CH_2, 5-CH_2), 1.98–2.06 (1 H, m, piperidine 2-C*H*H or 6-C*H*H), 2.34 (2 H, br, piperidine 2-C*H*H, 6-C*H*H), 2.49 (1 H, br, piperidine 2-C*H*H or 6-C*H*H), 2.61 (1 H, dt, *J* 11.4, 1.5, C*H*NBn$_2$), 2.68 (1 H, t, *J* 11.4, one of 1′-CH_2), 2.82 (1 H, dd, *J* 11.4, 1.5, one of 1′-CH_2), 3.44 (2 H, d, *J* 13.5, 2 × C*H*HPh), 3.81 (2 H, d, *J* 13.5, 2 × C*H*HPh), 3.93 (1 H, dt, *J* 8.9, 1.5, C*H*OH), 7.22–7.36 (10 H, m, Ar-H); δ_C(75 MHz; $CDCl_3$) 14.29 (CH_3), 18.23 (CH_2CH_3), 24.12, 25.91, 37.97 ($CH_2CH_2CH_3$), 54.27, 54.97, 55.20 (*C*HNBn$_2$), 57.47, 75.08 (CHOH), 127.03, 128.25, 128.79, 139.70; ν_{max}(thin film)/cm^{-1} 3500–3180 (br, s), 2930 (s), 2900 (m), 2880 (m), 1500 (w), 1480 (w), 1450 (s), 1350 (m), 1220 (s), 1100 (s), 1065 (m), 980 (w), 760 (s), 700 (m); *m/z* (EI) 380 (M^+, 4%), 362 (8), 337 (6), 319 (24), 307 (65), 294 (5), 282 (49), 264 (8), 236 (8), 181 (10), 132 (9), 106 (15), 91 (100), 69 (12), 57 (19) (Found: M^+, 380.282. Calc. for $C_{25}H_{36}N_2O$: *M*, 380.283).

(±)-1-[(2′*R,3′*S**)-2′-(*N*,*N*-Diallylamino)-3′-hydroxyhexyl]piperidine (entry 8).** From trimethylsilyl trifluoromethanesulfonate (0.29 g, 0.25 cm^3, 1.29 mmol), (±)-(2*S**,3*S**)-1-(*N*,*N*-diallylamino)-2,3-epoxyhexane and piperidine (0.18 g, 0.21 ml, 2.15 mmol); purified by column chromatography on flash silica (eluent 50% ethyl acetate–50% light petroleum) to give (±)-*N*-[(2′*R**,3′*S**)-2′-(*N*,*N*-diallylamino)-3′-hydroxyhexyl]piperidine (0.20 g, 0.71 mmol, 66%) as a pale yellow oil; δ_H(400 MHz; $CDCl_3$) 0.93 (3 H, t, *J* 7.2, CH_3), 1.25–1.41 (5 H, m, $CH_2CH_2CH_3$, piperidine 4-C*H*H), 1.54–1.61 (5 H, m, 3-CH_2, 5-CH_2, piperidine 4-C*H*H), 1.81–1.88 (1 H, m, piperidine 2-C*H*H or 6-C*H*H), 2.28 (2 H, br, piperidine 2-C*H*H, 6-C*H*H), 2.48 (1 H, dd, *J* 12.0, 9.0, one of 1′-CH_2), 2.57 (1 H, br, piperidine 2-C*H*H or 6-C*H*H), 2.58 (1 H, dd, *J* 12.0, 2.4, one of 1′-CH_2), 2.68 [1 H, dt, *J* 9.0, 2.4, C*H*N(allyl)$_2$], 2.89 (2 H, dd, *J* 14.2, 8.4, 2 × allylic C*H*H), 3.23 (2 H, dd, *J* 14.2, 4.3, 2 × allylic C*H*H), 3.77 (1 H, dt, *J* 9.0, 2.4, C*H*OH), 5.05–5.16 (4 H, m, CH=CH_2 × 2), 5.69–5.79 (2 H, m, CH=CH_2 × 2); δ_C(75 MHz; $CDCl_3$) 14.33 (CH_3), 18.49 (CH_2CH_3), 24.14, 25.95, 37.18 ($CH_2CH_2CH_3$), 53.22, 55.03, 56.40 [*C*HN(allyl)$_2$], 57.58, 75.46 (CHOH), 116.46 (2 C, CH=*C*H_2 × 2), 137.35 (2 C, *C*H=CH_2 × 2); ν_{max}(thin film)/cm^{-1} 3500–3180 (br, s), 2940 (s), 2860 (m), 2830 (m), 2810 (m), 1635 (m), 1450 (s), 1430 (s), 1370 (w), 1355 (w), 1340 (w), 1290 (w), 1260 (w), 1150 (w), 1005 (s), 990 (w), 970 (w), 910 (s), 850 (m); *m/z* (EI) 280 (M$^+$, 17%), 253 (17), 237 (41), 182 (100), 140 (36), 122 (11), 110 (7), 98 (59), 84 (7), 70 (16), 55 (15), 41 (29) (Found: C, 72.70; H, 11.60; N, 9.80. Calc. for $C_{17}H_{32}N_2O$: C, 72.86; H, 11.43; N, 10.00%).

(±)-4-[(2′*R,3′*S**)-2′-(*N*,*N*-Dibenzylamino)-3′-hydroxyhexyl]morpholine (entry 9).** From trimethylsilyl trifluoromethanesulfonate (0.33 g, 0.29 cm^3, 1.51 mmol), (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (0.37 g, 1.25 mmol) and morpholine (0.22 g, 0.22 ml, 2.51 mmol); purified by column chromatography on flash silica (eluent ethyl acetate) to give (±)-*N*-[(2′*R**,3′*S**)–2′-(*N*,*N*-dibenzylamino)-3′-hydroxyhexyl]-morpholine (0.44 g, 1.15 mmol, 92%) as a viscous yellow oil; δ_H(300 MHz; [$^2H_6$]acetone) 0.87 (3 H, t, *J* 6.6, CH_3), 1.25–1.36 (3 H, m, CH_2CH_3 and one of $CH_2CH_2CH_3$), 1.82–1.88 (1 H, m, remaining $CH_2CH_2CH_3$), 2.79 (5 H, br, morpholine 3-CH_2, 5-CH_2, $CHNBn_2$), 3.08 (1 H, br, one of 1′-CH_2), 3.24 (1 H, br, remaining 1′-CH_2), 3.62–3.73 (6 H, m, morpholine 2-CH_2, 6-CH_2, 2 × C*H*HPh), 3.85 (2 H, d, *J* 13.5, 2 × C*H*HPh), 4.07 (1 H, br, C*H*OH), 7.24–7.45 (10 H, m, Ar-H); δ_C(75 MHz; [$^2H_6$]acetone) 14.36 (CH_3), 18.78 (CH_2CH_3), 37.99 ($CH_2CH_2CH_3$), 54.09, 54.87, 56.78, 66.03, 72.46 (CHOH), 128.21, 129.27, 129.92, 139.72; ν_{max}(thin film)/cm^{-1} 3480–3180 (br, s), 2940 (s), 2920 (m), 2900 (m), 2840 (s), 2820 (s), 1600 (m), 1500 (m), 1450 (s), 1360 (m), 1300 (m), 1270 (w), 1120 (s), 1030 (w), 1000 (m), 960 (m), 905 (m), 860 (m), 750 (s), 700 (m); *m/z* (EI) 383 (M$^+$ + 1, 7%), 372 (15), 339 (6), 309 (3), 282 (84), 264 (6), 223 (6), 210 (10), 190 (13), 132 (9), 114 (5), 100 (24), 91 (100), 65 (12), 56 (9) (Found: C, 75.40; H, 9.00; N, 7.20. Calc. for $C_{24}H_{34}N_2O_2$: C, 75.39; H, 8.90; N, 7.33%).

(±)-4-[(2′*R,3′*S**)-2′-(*N*,*N*-Diallylamino)-3′-hydroxyhexyl]morpholine (entry 10).** From trimethylsilyl trifluoromethanesulfonate (0.37 g, 0.32 cm^3, 1.66 mmol), (±)-(2*S**,3*S**)-1-(*N*,*N*-diallylamino)-2,3-epoxyhexane (0.27 g, 1.39 mmol) and morpholine (0.24 g, 0.24 ml, 2.77 mmol); purified by column chromatography on flash silica (eluent ethyl acetate) to give (±)-*N*-[(2′*R**,3′*S**)-2′-(*N*,*N*-diallylamino)-3′-hydroxyhexyl]-morpholine (0.35 g, 1.24 mmol, 90%) as a yellow oil; δ_H(300 MHz; $CDCl_3$) 0.94 (3 H, t, *J* 6.9, CH_3), 1.26–1.41 (2 H, m, CH_2CH_3), 1.49–1.61 (1 H, m, one of $CH_2CH_2CH_3$), 1.81–1.88 (1 H, m, remaining $CH_2CH_2CH_3$), 2.31–2.73 [7 H, m, morpholine 3-CH_2, 5-CH_2, 1′-CH_2, C*H*N(allyl)$_2$], 2.91 (2 H, dd, *J* 13.2, 8.1, 2 × allylic C*H*H), 3.26 (2 H, dd, *J* 13.2, 1.5, 2 × allylic C*H*H), 3.69 (4 H, br, morpholine 2-CH_2, 6-CH_2), 3.78–3.87 (1 H, m, C*H*OH), 4.08 (1 H, br, OH), 5.04–5.27 (4 H, m, CH=CH_2 × 2), 5.69–5.82 (2 H, m, C*H*=CH_2 × 2); δ_C(75 MHz; $CDCl_3$) 14.24 (CH_3), 18.46 (CH_2CH_3), 37.12 ($CH_2CH_2CH_3$), 53.32, 54.04, 56.27 [*C*HN(allyl)$_2$], 57.65, 66.81, 75.43 (CHOH), 116.57 (2 C, CH=*C*H_2 × 2), 137.18 (2 C, *C*H=CH_2 × 2); ν_{max}(thin film)/cm^{-1} 3500–3180 (br, s), 2950 (s), 2910 (m), 2900 (m), 2870 (m), 2850 (m), 1620 (s), 1460 (s), 1440 (s), 1410 (s), 1365 (m), 1300 (w), 1120 (s), 1000 (w), 910 (m), 860 (s), 750 (s); *m/z* (EI) 283 (M$^+$ + 1, 10%), 255 (7), 239 (21), 209 (35), 182 (100), 140 (34), 122 (8), 100 (26), 81 (5), 70 (15), 56 (12), 41 (21) (Found: M$^+$, 282.230. Calc. for $C_{16}H_{30}N_2O_2$: *M*, 282.231).

(−)-4-[(2′*R*,3′*R*)-2′-(*N*,*N*-Diallylamino)-3′-hydroxy-4′-*tert*-butyldimethylsilyloxybutyl]morpholine (entry 11). From trimethylsilyl trifluoromethanesulfonate (0.25 g, 0.21 cm^3, 1.11 mmol), (2*S*,3*S*)-1-(*N*,*N*-diallylamino)-4-*tert*-butyldimethylsilyloxy-2,3-epoxybutane (0.33 g, 1.11 mmol) and morpholine (0.19 g, 0.19 cm^3, 2.22 mmol); purified by column chromatography on flash silica (eluent 50% ethyl acetate–50% light petroleum) to give 4-[(2′*R*,3′*R*)-2′-(*N*,*N*-diallylamino)-3′-hydroxy-4′-*tert*-butyldimethylsilyloxybutyl]morpholine (0.25 g, 0.65 mmol, 59%) as a viscous yellow oil; $[\alpha]_D^{20}$ −45.7 (*c* 1.12 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 0.08 [6 H, s, Si$(CH_3)_2$], 0.91 [9 H, s, C$(CH_3)_3$], 2.39 (2 H, br, morpholine 3-C*H*H, 5-C*H*H), 2.59–2.61 (4 H, m, 1′-CH_2, morpholine 3-C*H*H, 5-C*H*H), 2.94 (2 H, dd, *J* 14.4, 8.0, 2 × allylic C*H*H), 3.03 [1 H, dt, *J* 14.6, 8.1, C*H*N(allyl)$_2$], 3.28 (2 H, dd, *J* 14.4, 4.3, 2 × allylic C*H*H), 3.63–3.70 (5 H, m, morpholine 2-CH_2, 6-CH_2, one of CH_2OTBDMS), 3.75 (1 H, dt, *J* 8.1, 2.2, C*H*OH), 3.81 (1 H, dd, *J* 10.2, 2.2, one of CH_2OTBDMS), 5.06–5.16 (4 H, m, CH=CH_2 × 2), 5.70–5.80 (2 H, m, C*H*=CH_2 × 2), 5.88 (1 H, br, OH); δ_C(75 MHz; $CDCl_3$) −5.09 [2 C, Si$(CH_3)_2$], 18.44 (*C*Me$_3$), 26.02 [3 C, C(*C*$H_3)_3$], 52.29 [*C*HN(allyl)$_2$], 53.33, 53.82, 56.51, 65.55, 66.84, 75.35 (CHOH), 116.45 (2 C, CH=*C*H_2 × 2), 137.24 (2 C, *C*H=CH_2 × 2); ν_{max}(thin film)/cm^{-1} 3500–3200 (br, m), 2920 (s), 2840 (s), 2800 (m), 1630 (w), 1450 (s), 1400 (w), 1350 (m), 1250 (s), 1110 (s), 990 (s), 910 (s), 830 (s), 770 (s), 670 (m); *m/z* (EI) 384 (M$^+$, 6%), 369 (32), 357 (10), 343 (37), 328 (42), 284 (100), 122 (6), 110 (22), 100 (41), 89 (18), 73 (34), 56 (11), 41 (22) (Found: C, 62.25; H, 10.30; N, 7.35. Calc. for $C_{20}H_{40}N_2O_3Si$: C, 62.50; H, 10.42; N, 7.29%).

(−)-4-[(2′*R*,3′*R*)-2′-(*N*,*N*-Dibenzylamino)-3′-hydroxyhexyl]morpholine (entry 12). From trimethylsilyl trifluoromethanesulfonate (0.33 g, 0.29 cm^3, 1.51 mmol), (+)-(2*S*,3*R*)-(*N*,*N*-dibenzylamino)-2,3-epoxyhexylamine (0.37 g, 1.25 mmol) and morpholine (0.22 g, 0.22 cm^3, 2.51 mmol); purified by column chromatography on flash silica (eluent ethyl acetate) to give (−)-4-[(2′*R*,3′*R*)-2′-(*N*,*N*-dibenzylamino)-3′-hydroxyhexyl]-morpholine (0.28 g, 0.73 mmol, 58%) as a viscous yellow oil; $[\alpha]_D^{20}$ −24.1 (*c* 1.16 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 0.87 (3 H, t, *J* 7.0, CH_3), 1.34–1.44 (2 H, m, CH_2CH_3), 1.55–1.62 (1 H, m, one of $CH_2CH_2CH_3$), 1.74–1.80 (1 H, m, one of $CH_2CH_2CH_3$), 2.14 (1 H, t, *J* 12.1, C*H*NBn$_2$), 2.35–2.46 (4 H, m, 1′-CH_2, morpholine 3-C*H*H, 5-C*H*H), 2.63–2.68 (2 H, m, morpholine 3-C*H*H, 5-C*H*H), 3.60 (2 H, d, *J* 13.8, 2 × C*H*HPh), 3.65–3.74 (4 H, m, morpholine 2-CH_2, 6-CH_2), 3.77 (2 H, d, *J* 13.8, 2 × C*H*HPh), 3.98 (1 H, dd, *J* 7.8, 4.1, C*H*OH), 7.21–7.35 (10 H, Ar-H); δ_C(75 MHz; $CDCl_3$) 14.47 (CH_3), 21.01 (CH_2CH_3), 28.63 ($CH_2CH_2CH_3$), 53.53, 54.71, 59.94 (*C*HNBn$_2$), 63.09, 64.94 (CHOH), 66.97, 126.78, 128.13, 128.93, 140.30; ν_{max}(thin film)/cm^{-1} 3520–3340 (br, m), 3020 (m), 2940 (s), 2800 (s), 1600 (w), 1480 (m), 1440 (s), 1360 (m), 1290 (m), 1260 (m), 1110 (s), 1060 (m), 1020 (m), 1000 (m), 960 (m), 910 (m), 860 (m), 740 (s), 690 (s); *m/z* (EI) 383 (M$^+$ + 1, 14%), 321 (34), 291 (26), 282 (34), 252 (91), 210 (10), 196 (7), 181 (21), 168 (24), 142 (9), 130 (34), 100 (65), 91 (100), 65 (21), 56 (28) (Found: M$^+$, 382.263. Calc. for $C_{24}H_{34}N_2O_2$: *M*, 382.262).

(±)-(2*R,3*S**)-1-(*N*,*N*-Diallylamino)-2-(*N*,*N*-dibenzylamino)hexan-3-ol (entry 13).** From trimethylsilyl trifluoromethanesulfonate (0.24 g, 0.20 cm^3, 1.06 mmol), (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (0.26 g, 0.88 mmol) and diallylamine (0.17 g, 0.22 cm^3, 1.76 mmol); purified by column chromatography on flash silica (eluent 20% ethyl acetate–80% light petroleum) to give (±)-(2*R**,3*S**)-1-(*N*,*N*-diallyl-

amino)-2-(*N*,*N*-dibenzylamino)hexan-3-ol (0.23 g, 0.59 mmol, 67%) as a yellow oil; δ_H(300 MHz; $CDCl_3$) 0.92 (3 H, t, *J* 6.6, CH_3), 1.23–1.43 (3 H, m, CH_2CH_3, one of $CH_2CH_2CH_3$), 1.94–1.99 (1 H, m, remaining $CH_2CH_2CH_3$), 2.61 (1 H, dt, *J* 11.1, 2.4, CHNBn$_2$), 2.78–2.89 [4 H, m, 2 × allylic CH, CH_2N(allyl)$_2$], 3.26 (2 H, dd, *J* 13.5, 4.2, 2 × allylic CH), 3.44 (2 H, d, *J* 13.8, 2 × CHPh), 3.78 (2 H, d, *J* 13.5, 2 × CHPh), 3.88–3.94 (1 H, m, CHOH), 5.13–5.19 (4 H, m, CH=CH_2 × 2), 5.72–5.85 (2 H, m, CH=CH_2 × 2), 7.19–7.37 (10 H, m, Ar-H); δ_C(75 MHz; $CDCl_3$) 14.24 (CH_3), 18.13 (CH_2CH_3), 36.87 ($CH_2CH_2CH_3$), 51.91, 54.23, 55.81 (CHNBn$_2$), 56.58, 74.90 (CHOH), 118.83 (2 C, CH=CH_2 × 2), 126.98, 128.18, 128.67, 133.86 (2 C, CH=CH_2 × 2), 139.59; ν_{max}(thin film)/cm^{-1} 3440–3160 (br, s), 2960 (s), 2920 (s), 2800 (s), 1665 (m), 1640 (m), 1600 (m), 1485 (m), 1465 (s), 1370 (m), 1325 (w), 1250 (w), 1200 (w), 1100 (s), 1060 (w), 990 (w), 970 (w), 920 (m), 840 (w), 740 (s), 690 (m); *m*/*z* (EI) 392 (M^+, 10%), 351 (6), 319 (30), 301 (42), 282 (67), 265 (7), 236 (16), 223 (6), 181 (11), 132 (12), 110 (17), 91 (100), 65 (9), 49 (24), 41 (16) (Found: C, 79.75; H, 9.40; N, 7.35. Calc. for $C_{26}H_{36}N_2O$: C, 79.59; H, 9.18; N, 7.14%).

(±)-(2*R,3*S**)-1,2-bis(*N*,*N*-Diallylamino)hexan-3-ol (entry 14).** From trimethylsilyl trifluoromethanesulfonate (0.41 g, 0.36 cm^3, 1.85 mmol), (±)-(2*S**,3*S**)-1-(*N*,*N*-diallylamino)-2,3-epoxyhexane (0.30 g, 1.54 mmol) and diallylamine (0.30 g, 0.38 cm^3, 3.08 mmol); purified by column chromatography on flash silica (eluent 20% ethyl acetate–80% light petroleum) to give (±)-(2*R**,3*S**)-1,2-bis(*N*,*N*-diallylamino)hexan-3-ol (0.40 g, 1.37 mmol, 89%) as a yellow oil; δ_H(300 MHz; $CDCl_3$) 0.93 (3 H, t, *J* 6.9, CH_3), 1.23–1.41 (2 H, m, CH_2CH_3), 1.51–1.61 (1 H, m, one of $CH_2CH_2CH_3$), 1.78–1.86 (1 H, m, remaining $CH_2CH_2CH_3$), 2.59–2.75 [3 H, m, CHN(allyl)$_2$, CH_2N(allyl)$_2$], 2.84 (2 H, dd, *J* 14.1, 7.8, 2 × allylic CH), 2.91 (2 H, dd, *J* 14.1, 7.8, 2 × allylic CH), 3.24 (2 H, dd, *J* 14.1, 2.1, 2 × allylic CH), 3.34 (2 H, dd, *J* 14.1, 5.1, 2 × allylic CH), 3.78 (1 H, dt, *J* 6.3, 1.5, CHOH), 5.06–5.21 (8 H, m, CH=CH_2 × 4), 5.69–5.90 (4 H, m, CH=CH_2 × 4), 6.48 (1 H, br, OH); δ_C(75 MHz; $CDCl_3$) 14.32 (CH_3), 18.45 (CH_2CH_3), 37.17 ($CH_2CH_2CH_3$), 52.21, 53.36, 56.86, 57.40 [CHN(allyl)$_2$], 75.28 (CHOH), 116.33 (2 C, CH=CH_2 × 2), 118.61 (2 C, CH=CH_2 × 2), 134.23 (2 C, CH=CH_2 × 2), 137.41 (2 C, CH=CH_2 × 2); ν_{max}(thin film)/cm^{-1} 3480–3160 (br, s), 2940 (s), 2910 (s), 2890 (m), 2810 (m), 1635 (m), 1440 (s), 1410 (s), 1360 (w), 1340 (m), 1330 (m), 1150 (w), 1105 (s), 990 (w), 960 (w), 910 (s), 850 (m); *m*/*z* (EI) 292 (M^+, 17%), 263 (23), 251 (75), 236 (30), 223 (80), 218 (55), 205 (32), 195 (38), 182 (100), 140 (37), 122 (10), 110 (34), 96 (5), 81 (10), 70 (15), 55 (11), 41 (44) (Found: C, 73.70; H, 10.80; N, 9.35. Calc. for $C_{18}H_{32}N_2O$: C, 73.97; H, 10.96; N, 9.59%).

(±)-(2*R,3*S**)-2-(*N*,*N*-Dibenzylamino)-1-(*N*-butylamino)hexan-3-ol (entry 15).** From trimethylsilyl trifluoromethanesulfonate (0.26 g, 0.23 cm^3, 1.18 mmol), (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (0.29 g, 0.98 mmol) and butylamine (0.14 g, 0.19 cm^3, 1.97 mmol); purified by column chromatography on flash silica (eluent ethyl acetate) to give (±)-(2*R**,3*S**)-2-(*N*,*N*-dibenzylamino)-1-(*N*-butylamino)hexan-3-ol (0.16 g, 0.43 mmol, 44%) as a colourless oil; δ_H(300 MHz; $CDCl_3$) 0.87–0.94 (6 H, m, CH_3 × 2), 1.22–1.47 (7 H, m, $NHCH_2CH_2$, CH_2CH_3, one of $CH_2CH_2CH_3$), 1.90–1.91 (1 H, m, one of $CH_2CH_2CH_3$), 2.45–2.64 (3 H, m, $NHCH_2CH_2$, CHNBn$_2$), 2.83 (1 H, t, *J* 11.0, one of CH_2NH), 3.22 (1 H, dd, *J* 11.0, 2.4, one of CH_2NH), 3.49 (2 H, d, *J* 13.5, 2 × CHPh), 3.80 (2 H, d, *J* 13.5, 2 × CHPh), 3.96–3.99 (1 H, m, CHOH), 7.22–7.43 (10 H, m, Ar-H); δ_C(75 MHz; $CDCl_3$) 13.88, 14.23, 18.18, 20.30, 31.70, 37.46, 47.66, 49.27, 54.50, 58.97 (CHNBn$_2$), 74.09 (CHOH), 127.01, 128.20, 128.78, 139.64; ν_{max}(thin film)/cm^{-1} 3500–3200 (br, s), 2940 (s), 2910 (s), 2840 (m), 1480 (m), 1445 (s), 1360 (m), 1240 (w), 1110 (s), 1060 (m), 1015 (m), 960 (w), 740 (m), 685 (s); *m*/*z* (EI) 369 (M^+ + 1, 61%), 349 (57), 324 (33), 307 (29), 282 (65), 265 (17), 252 (19), 236 (22), 223 (13), 210 (5), 181 (11), 154 (6), 132 (19), 106 (6), 91 (100), 65 (12), 41 (8) (Found: C, 78.35; H, 9.60; N, 7.80. Calc. for $C_{24}H_{36}N_2O$: C, 78.26; H, 9.78; N, 7.61%).

(±)-(2*R,3*S**)-2-(*N*,*N*-Dibenzylamino)-1-(*N*-isopropylamino)hexan-3-ol (entry 16).** From trimethylsilyl trifluoromethanesulfonate (0.29 g, 0.25 cm^3, 1.31 mmol), (±)-(2*S**,3*S**)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (0.32 g, 1.08 mmol) and isopropylamine (0.13 g, 0.18 cm^3, 2.16 mmol); purified by column chromatography on flash silica (eluent ethyl acetate) to give (±)-(2*R**,3*S**)-2-(*N*,*N*-dibenzylamino)-1-(*N*-isopropylamino)hexan-3-ol (0.18 g, 0.51 mmol, 47%) as a yellow oil; δ_H(300 MHz; $CDCl_3$) 0.93 (3 H, t, *J* 6.9, CH_2CH_3), 1.07 [3 H, d, *J* 6.3, one of $CH(CH_3)_2$], 1.09 [3 H, d, *J* 6.3, remaining $CH(CH_3)_2$], 1.26–1.38 (3 H, m, CH_2CH_3, one of $CH_2CH_2CH_3$), 1.85–1.90 (1 H, m, one of $CH_2CH_2CH_3$), 2.53 (1 H, dt, *J* 9.3, 3.6, CHNBn$_2$), 2.73 [1 H, septet, *J* 6.3, $CH(CH_3)_2$], 2.85 (1 H, t, *J* 9.3, one of CH_2NH), 3.20 (1 H, dd, *J* 9.3, 3.6, one of CH_2NH), 3.55 (2 H, d, *J* 13.8, 2 × CHPh), 3.79 (2 H, d, *J* 13.8, 2 × CHPh), 3.97 (1 H, dt, *J* 8.1, 3.6, CHOH), 7.21–7.35 (10 H, m, Ar-H); δ_C(75 MHz; $CDCl_3$) 14.19 (CH_2CH_3), 18.28 (CH_2CH_3), 21.75 [one of $CH(CH_3)_2$], 22.39 [remaining $CH(CH_3)_2$], 37.61 ($CH_2CH_2CH_3$), 44.74, 49.20 [$CH(CH_3)_2$], 54.56, 59.86 (CHNBn$_2$), 73.66 (CHOH), 127.13, 128.35, 128.80, 139.51; ν_{max}(thin film)/cm^{-1} 3540–3200 (br, s), 2960 (s), 2840 (m), 2820 (m), 1645 (w), 1630 (w), 1600 (m), 1485 (m), 1450 (s), 1380 (s), 1290 (m), 1240 (s), 1150 (m), 1105 (s), 1025 (m), 970 (m), 905 (w), 880 (w), 830 (m), 740 (s), 690 (m), 640 (m); *m*/*z* (EI) 355 (M^+ + 1, 10%), 282 (89), 265 (25), 236 (27), 223 (9), 210 (5), 190 (13), 132 (16), 91 (100), 65 (15), 55 (8), 43 (16) (Found: M^+, 354.267. Calc. for $C_{23}H_{34}N_2O$: *M*, 354.267).

(±)-(2*R,3*S**)-2-(*N*,*N*-Diallylamino)-1-(*N*-isopropylamino)-hexan-3-ol (entry 17).** From trimethylsilyl trifluoromethanesulfonate (0.29 g, 0.25 cm^3, 1.29 mmol), (±)-(2*S**,3*S**)-1-(*N*,*N*-diallylamino)-2,3-epoxyhexane (0.21 g, 1.08 mmol) and isopropylamine (0.13 g, 0.18 cm^3, 2.16 mmol); purified by column chromatography on flash silica (eluent ethyl acetate) to give (±)-(2*R**,3*S**)-2-(*N*,*N*-diallylamino)-1-(*N*-isopropylamino)hexan-3-ol (0.13 g, 0.51 mmol, 47%) as a yellow oil; δ_H(300 MHz; $CDCl_3$) 0.93 (3 H, t, *J* 7.2, CH_2CH_3), 1.08 [6 H, d, *J* 6.3, $CH(CH_3)_2$], 1.30–1.40 (2 H, m, CH_2CH_3), 1.53–1.56 (1 H, m, one of $CH_2CH_2CH_3$), 1.73–1.77 (1 H, m, one of $CH_2CH_2CH_3$), 2.50 [1 H, dt, *J* 8.0, 3.0, CHN(allyl)$_2$], 2.70 (1 H, dd, *J* 11.4, 8.0, one of CH_2NH), 2.77 [1 H, septet, *J* 6.3, $CH(CH_3)_2$], 2.98–3.07 (3 H, m, one of CH_2NH, and 2 × allylic CH), 3.26 (2 H, dd, *J* 14.4, 5.1, 2 × allylic CH), 3.83 (1 H, dt, *J* 8.1, 3.0, CHOH), 5.07–5.18 (4 H, m, CH=CH_2 × 2), 5.71–5.84 (2 H, m, CH=CH_2 × 2); δ_C(75 MHz; $CDCl_3$) 14.27 (CH_2CH_3), 18.61 (CH_2CH_3), 22.34 [one of $CH(CH_3)_2$], 22.88 [remaining $CH(CH_3)_2$], 37.84 ($CH_2CH_2CH_3$), 45.07, 48.91 [$CH(CH_3)_2$], 53.36, 60.83 [CHN(allyl)$_2$], 74.15 (CHOH), 116.50 (2 C, CH=CH_2 × 2), 137.06 (2 C, CH=CH_2 × 2); ν_{max}(thin film)/cm^{-1} 3520–3120 (br, s), 2970 (s), 2930 (m), 2910 (m), 2870 (m), 1640 (m), 1460 (s), 1440 (s), 1410 (m), 1380 (m), 1370 (m), 1350 (m), 1270 (m), 1160 (m), 1100 (m), 1030 (w), 1000 (w), 920 (s), 850 (w); *m*/*z* (EI) 255 (M^+ + 1, 8%), 239 (10), 225 (12), 214 (9), 198 (7), 182 (95), 164 (12), 152 (41), 140 (30), 123 (26), 110 (69), 96 (17), 81 (23), 69 (61), 55 (32), 41 (100) (Found: M^+, 254.237. Calc. for $C_{15}H_{30}N_2O$: *M*, 254.236).

(−)-(2*R*,3*S*)-1-Amino-2-(*N*,*N*-dibenzylamino)hexan-3-ol (entry 18). From trimethylsilyl trifluoromethanesulfonate (0.81 g, 0.71 cm^3, 3.66 mmol), (−)-(2*S*,3*S*)-1-(*N*,*N*-dibenzylamino)-2,3-epoxyhexane (0.90 g, 3.05 mmol). Liquid ammonia (large excess) was added periodically (reaction vessel was fitted with −78 °C condenser). After 36 h, the reaction was worked up in the usual manner. The crude product was purified by column chromatography on flash silica (eluent 80% $CHCl_3$–20% MeOH) to give (−)-(2*R*,3*S*)-1-amino-2-(*N*,*N*-dibenzylamino)-hexan-3-ol (0.62 g, 1.99 mmol, 65%) as a colourless viscous oil: $[\alpha]_D^{24}$ −29.5 (*c* 1.22, in $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 0.92 (3 H, t, *J* 7.5, CH_3), 1.27–1.40 (3 H, m, CH_2CH_3, one of $CH_2CH_2CH_3$), 1.75–1.81 (1 H, m, remaining $CH_2CH_2CH_3$), 2.43 (1 H, dt, *J*

9.0, 5.0, C*H*NBn$_2$), 2.57 (2 H, br s, NH$_2$), 2.89 (1 H, dd, *J* 12.0, 9.0, one of C*H*$_2$NH$_2$), 3.30 (1 H, dd, *J* 12.0, 5.0, remaining C*H*$_2$NH$_2$), 3.58 (2 H, d, *J* 13.5, 2 × C*H*HPh), 3.75 (2 H, d, *J* 13.5, 2 × C*H*HPh), 3.97–4.02 (1 H, m, C*H*OH), 7.20–7.23 (10 H, m, Ar-H); δ_C(75 MHz; $CDCl_3$) 14.22 (CH$_2$*C*H$_3$), 18.40 (*C*H$_2$CH$_3$), 37.80 (*C*H$_2$CH$_2$CH$_3$), 39.70, 54.62, 61.62 (*C*HNBn$_2$), 73.33 (*C*HOH), 126.98, 128.25, 128.79, 139.79; ν_{max}(thin film)/cm^{-1} 3500–3180 (br, s), 2960 (s), 2940 (s), 2880 (s), 1640 (w), 1600 (m), 1485 (m), 1445 (s), 1370 (m), 1360 (m), 1330 (w), 1270 (w), 1240 (w), 1210 (w), 1105 (m), 1025 (w), 970 (m), 910 (w), 850 (m), 740 (s), 690 (m); *m/z* (EI) 313 (M$^+$ + 1, 33%), 296 (10), 282 (74), 239 (36), 181 (18), 132 (7), 120 (5), 106 (8), 91 (100), 65 (27), 55 (9), 43 (12) (Found: C, 77.00; H, 9.10; N, 8.80. Calc. for $C_{20}H_{28}N_2O$: C, 76.92; H, 8.97; N, 8.97%).

(±)-(2*R,3*S**)-1-Amino-2-(*N*,*N*-diallylamino)hexan-3-ol (entry 19).** From trimethylsilyl trifluoromethanesulfonate (0.79 g, 0.69 cm^3, 3.57 mmol), (±)-(2*S**,3*S**)-1-(*N*,*N*-diallylamino)-2,3-epoxyhexane (0.58 g, 2.97 mmol) as for entry 18. This gave (±)-(2*R**,3*S**)-1-amino-2-(*N*,*N*-diallylamino)hexan-3-ol (0.34 g, 1.60 mmol, 54%) as a viscous yellow oil; δ_H(300 MHz; $CDCl_3$) 0.93 (3 H, t, *J* 7.5, CH$_3$), 1.33–1.41 (2 H, m, C*H*$_2$CH$_3$), 1.50–1.55 (1 H, m, one of C*H*$_2$CH$_2$CH$_3$), 1.66–1.69 (1 H, m, remaining C*H*$_2$CH$_2$CH$_3$), 2.49 [1 H, dt, *J* 9.0, 3.0, C*H*N(allyl)$_2$], 2.72 (2 H, br, NH$_2$), 2.83 (1 H, dd, *J* 12.0, 9.0, one of C*H*$_2$NH$_2$), 3.08 (2 H, dd, *J* 13.5, 9.0, 2 × allylic C*H*H), 3.17–3.22 (1 H, m, remaining C*H*$_2$NH$_2$), 3.23 (2 H, dd, *J* 13.5, 6.0, 2 × allylic C*H*H), 3.83–3.86 (1 H, m, C*H*OH), 5.07–5.17 (4 H, m, CH=C*H*$_2$ × 2), 5.71–5.82 (2 H, m, C*H*=CH$_2$ × 2); δ_C(75 MHz; $CDCl_3$) 14.23 (CH$_2$*C*H$_3$), 18.75 (*C*H$_2$CH$_3$), 37.83 (*C*H$_2$-CH$_2$CH$_3$), 40.02, 53.47, 62.77 [*C*HN(allyl)$_2$], 73.52 (CHOH), 116.47 (2 C, CH=*C*H$_2$ × 2), 137.1 (2 C, *C*H=CH$_2$ × 2); ν_{max}-(thin film)/cm^{-1} 3500–3100 (br, s), 2960 (s), 2900 (m), 2860 (s), 1640 (s), 1600 (w), 1590 (w), 1560 (w), 1460 (s), 1415 (m), 1380 (w), 1350 (w), 1140 (m), 1095 (s), 1065 (m), 995 (w), 920 (s), 850 (m), 750 (s), 660 (w); *m/z* (EI) 212 (M$^+$, 20%), 197 (11), 182 (100), 152 (7), 140 (49), 122 (14), 110 (26), 96 (17), 83 (9), 70 (31), 56 (15) (Found: M$^+$, 212.188. Calc. for $C_{12}H_{24}N_2O$: *M*, 212.189).

Synthesis of (−)-(2′*R*,3′*S*)-2,6-diacetamido-4-[2′-(*N*,*N*-dibenzylamino)-3′-hydroxyhexylamino]pyrimidine 21 (Scheme 7)[49]

(−)-(2*R*,3*S*)-1-Amino-2-(*N*,*N*-dibenzylamino)hexan-3-ol **19** (0.24 g, 0.77 mmol), 2,6-diacetamido-4-chloropyrimidine **20** (0.14 g, 0.59 mmol) and triethylamine (0.08 g, 0.11 cm^3, 0.77 mmol) were added to acetonitrile (3 cm^3). The reaction mixture was heated to 80 °C for 72 h and then cooled. Acetonitrile was removed *in vacuo*. The product was purified first by column chromatography on flash silica (eluent ethyl acetate) followed by recrystallisation (MeCN) to give (−)-(2′*R*,3′*S*)-2,6-diacetamido-4-[2′-(*N*,*N*-dibenzylamino)-3′-hydroxyhexylamino]pyrimidine (0.16 g, 0.32 mmol, 42%) as a white solid; mp 181.3–182.6 °C (MeCN); $[a]_D^{16}$ −65.9 (*c* 1.02, in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 0.96 (3 H, t, *J* 7.2, CH$_2$C*H*$_3$), 1.26–1.40 (1 H, m, one of C*H*$_2$CH$_3$), 1.42–1.49 (2 H, m, one of C*H*$_2$CH$_3$, one of C*H*$_2$CH$_2$CH$_3$), 1.55–1.62 (1 H, m, one of C*H*$_2$CH$_2$CH$_3$), 1.89 (1 H, br, s, CH$_2$N*H*), 2.25 (3 H, s, 6-NHCOC*H*$_3$), 2.62 (3 H, s, 2-NHCOC*H*$_3$), 2.73 (1 H, br, C*H*NBn$_2$), 3.63 (2 H, d, *J* 13.6, 2 × C*H*HPh), 3.61–3.65 (2 H, m, 3.63, C*H*$_2$NH), 3.88 (2 H, d, *J* 13.6, 2 × C*H*HPh), 4.09 (1 H, br, C*H*OH), 7.06 (1 H, s, 5-H), 7.20–7.33 (10 H, Ar-H), 10.40 (1 H, br, 6-N*H*COCH$_3$), 10.59 (1 H, br, 2-N*H*COCH$_3$); δ_C(75 MHz; $CDCl_3$) 13.98 (CH$_2$*C*H$_3$), 18.95 (*C*H$_2$CH$_3$), 24.51, 25.64, 37.92, 38.25, 54.40, 60.62 (*C*HNBn$_2$), 69.90 (CHOH), 127.22, 128.45, 128.83, 139.50, 164.07, 170.90; ν_{max}(CH_2Cl_2)/cm^{-1} 3250–3160 (br, m), 2920 (m), 2880 (m), 1650 (m), 1600 (s), 1570 (s), 1430 (m), 1350 (m), 1300 (s), 1230 (s), 1050 (w), 1010 (w), 810 (m), 730 (m), 680 (m); *m/z* (FAB) 505 (M$^+$ + 1, 100%), 431 (19), 413 (9), 282 (54), 222 (7), 210 (14), 91 (93) (Found: M + H, 505.293. Calc. for $C_{28}H_{37}N_6O_3$: *M*, 505.293).

Synthesis of 27 (Scheme 8)

4,7-Dihydro-2-dodecyl-1,3-dioxepine[16]

Tridecanal (5.00 g, 90% purity, 5.99 cm^3, 22.7 mmol), *cis*-but-2-en-1,4-diol (2.40 g, 2.20 cm^3, 27.3 mmol) and toluene-*p*-sulfonic acid (0.10 g) were heated under reflux in benzene (50 ml) with azeotropic removal of water. After 5 h production of water had ceased and the reaction was allowed to cool. The mixture was then washed with 1 M NaOH (2 × 30 cm^3), dried (MgSO$_4$), filtered and concentrated, the product was purified by column chromatography on flash silica (11:1 light petroleum–ethyl acetate) to give 4,7-dihydro-2-dodecyl-1,3-dioxepine (5.95 g, 22.2 mmol, 98%) as a colourless oil; δ_H(300 MHz; $CDCl_3$) 0.88 (3 H, t, *J* 6.9, CH$_3$), 1.26 (20 H, br s, [C*H*$_2$]$_{10}$CH$_3$), 1.60–1.68 (2 H, m, C*H*$_2$[CH$_2$]$_{10}$CH$_3$), 4.16 (2 H, d, *J* 15.0, 2 × OC*H*H), 4.39 (2 H, d, *J* 15.0, 2 × OC*H*H), 4.76 (1 H, t, *J* 5.4, C*H*[CH$_2$]$_{11}$CH$_3$), 5.72 (2 H, s, CH=CH); δ_C(75 MHz; $CDCl_3$) 14.14 (CH$_3$), 22.71, 24.82, 29.37–29.66 (7 C), 31.93, 33.57, 65.04 (2 C, OCH$_2$), 104.53 (*C*H[CH$_2$]$_{11}$CH$_3$), 129.81 (2 C, CH=CH); ν_{max}(thin film)/cm^{-1} 2900 (s), 2820 (m), 1710 (m), 1440 (s), 1370 (m), 1250 (w), 1185 (w), 1100 (s), 1085 (w), 1070 (w), 1040 (w), 995 (w), 900 (w); *m/z* (EI) 267 (M$^+$ − 1, 7%), 197 (10), 111 (8), 99 (100), 83 (16), 71 (56), 57 (31), 43 (61) (Found: C, 76.25; H, 12.20. Calc. for $C_{17}H_{32}O_2$: C, 76.12; H, 11.94%).

(*Z*)-4-Tridecyloxybut-2-en-1-ol[41]

To diethyl ether in a 250 ml three-necked round-bottomed flask equipped with condenser and pressure equalised dropping funnel under nitrogen was added anhydrous aluminium chloride (5.79 g, 43.4 mmol) portionwise *via* a solid addition flask. The solution was cooled to 0 °C and lithium aluminium hydride (0.44 g, 11.6 mmol) was added portionwise *via* a solid addition flask over 5 min. After stirring at 0 °C for 30 min, a solution of 4,7-dihydro-2-dodecyl-1,3-dioxepine (5.90 g, 22.0 mmol) in diethyl ether (60 cm^3) was added dropwise and the mixture stirred at 0 °C for 30 min. The cooling bath was then removed and the reaction mixture warmed to room temperature and stirred for a further 2 h. The solution was recooled to 0 °C and 10% aqueous sulfuric acid (35 cm^3) added dropwise over 20 min. The layers were then separated and the organic layer washed with water (20 cm^3) and saturated aqueous sodium hydrogen carbonate (10 cm^3), dried (MgSO$_4$), filtered and concentrated. The crude product was purified by column chromatography on flash silica (1:1 light petroleum–ethyl acetate) to give (*Z*)-4-tridecyloxybut-2-en-1-ol (5.40 g, 20.0 mmol, 91%) as a colourless oil; δ_H(400 MHz; $CDCl_3$) 0.87 (3 H, t, *J* 6.7, CH$_3$), 1.24–1.29 (20 H, m, [C*H*$_2$]$_{10}$CH$_3$), 1.54–1.61 (2 H, m, C*H*$_2$[CH$_2$]$_{10}$CH$_3$), 2.29 (1 H, br s, OH), 3.43 (2 H, t, *J* 6.7, C*H*$_2$[CH$_2$]$_{11}$CH$_3$), 4.03 (2 H, d, *J* 7.2, 4-H), 4.19 (2 H, d, *J* 6.2, 1-H), 5.67–5.73 (1 H, m, 3-H), 5.78–5.84 (1 H, m, 2-H); δ_C(75 MHz; $CDCl_3$) 14.12 (CH$_3$), 22.68, 26.15, 29.35–29.65 (8 C), 31.91, 58.75, 66.44, 70.88, 128.52, 132.02; ν_{max}(thin film)/cm^{-1} 3450–3250 (s, br), 2900 (s), 2880 (s), 1710 (m), 1450 (s), 1100 (s), 1010 (m), 710 (w); *m/z* (EI) no M$^+$ detected, 252 (9%), 239 (7), 211 (12), 197 (7), 154 (11), 125 (15), 111 (31), 97 (58), 83 (81), 70 (100), 57 (11), 43 (40) (Found: C, 75.55; H, 12.85. Calc. for $C_{17}H_{34}O_2$: C, 75.56; H, 12.59%).

(−)-(2*S*,3*R*)-3-Tridecyloxymethyloxirane-2-methanol

A procedure similar to (−)-(2*S*,3*R*)-3-propyloxirane-2-methanol using L-(+)-diethyl tartrate (4.04 g, 3.40 cm^3, 19.6 mmol), (*Z*)-4-tridecyloxybut-2-en-1-ol (5.30 g, 19.6 mmol), titanium(IV) isopropoxide (5.57 g, 5.80 cm^3, 19.6 mmol), *tert*-butyl hydroperoxide (13.9 cm^3, 39.3 mmol, 2.83 mol dm^{-3} in toluene), 4 Å molecular sieves (5 g) and dichloromethane (200 cm^3) after 6 days, gave the crude product which was purified by column chromatography on flash silica (1:1 light petroleum–ethyl acetate) to give (−)-(2*S*,3*R*)-3-tridecyloxymethyloxirane-2-methanol (4.26 g, 14.9 mmol, 76%) as a white solid; mp 73.1–74.5 °C; $[a]_D^{20}$ −7.2 (*c* 1.22 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 0.87

(3 H, t, *J* 6.6, CH_3), 1.25–1.31 (20 H, m, $[CH_2]_{10}CH_3$), 1.54–1.61 (2 H, m, $CH_2[CH_2]_{10}CH_3$), 2.35 (1 H, br s, OH), 3.21–3.27 (2 H, m, H-2, H-3), 3.44 (1 H, dt, *J* 9.2, 6.8, one of $CH_2[CH_2]_{11}CH_3$), 3.51 (1 H, dt, *J* 9.2, 6.7, one of $CH_2[CH_2]_{11}CH_3$), 3.60 (1 H, dd, *J* 11.0, 4.8, one of $CH_2O[CH_2]_{12}CH_3$), 3.67 (1 H, dd, *J* 11.0, 5.8, one of $CH_2O[CH_2]_{12}CH_3$), 3.70–4.48 (2 H, m, CH_2OH); δ_C(75 MHz; $CDCl_3$) 14.11 (CH_3), 22.68, 26.04, 29.34–29.63 (8 C), 31.91, 54.63 (C-2 or C-3), 55.60 (C-2 or C-3), 60.80, 68.73, 71.82; ν_{max}($CHCl_3$)/cm^{-1} 3500–3400 (br, m), 2900 (s), 2840 (m), 1720 (m), 1460 (m), 1200 (m), 1100 (s); *m/z* (EI) 287 (M^+ + 1%), 255 (32), 199 (10), 125 (7), 111 (14), 97 (23), 85 (30), 73 (100), 57 (79), 43 (76) (Found: M^+ + H, 287.259. Calc. for $C_{24}H_{41}SO_5$: *M*, 287.259).

(2*S*,3*R*)-3-Tridecyloxymethyloxiran-2-ylmethyl acetate (enantiomeric excess determination)

(−)-(2*S*,3*R*)-3-Tridecyloxymethyloxirane-2-methanol (0.10 g, 0.35 mmol) and acetic anhydride (0.07 g, 0.07 cm^3, 0.70 mmol) were stirred in pyridine (2 cm^3) at room temperature for 5 h. The reaction mixture was washed with 1 M sulfuric acid (2 × 7 cm^3) and extracted with dichloromethane (3 × 15 cm^3). The extracts were dried (Na_2SO_4), concentrated and the product was purified by column chromatography on flash silica (eluent 2:1 light petroleum–ethyl acetate) to give (2*S*,3*R*)-3-tridecyloxymethyloxiran-2-ylmethyl acetate (0.10 g, 0.31 mmol, 86%) as a white solid; δ_H(300 MHz; $CDCl_3$) 0.88 (3 H, t, *J* 6.6, CH_2CH_3), 1.24–1.26 (20 H, m, $[CH_2]_{10}CH_3$), 1.54–1.60 (2 H, m, $CH_2[CH_2]_{10}CH_3$), 2.11 (3 H, s, CH_3), 3.25–3.27 (2 H, m, 2-H, 3-H), 3.44–3.57 (3 H, m, $CH_2[CH_2]_{11}CH_3$ and one of OCH_2), 3.67 (1 H, dd, *J* 8.4, 0.6, one of OCH_2), 4.06 (1 H, dd, *J* 9.9, 1.3, one of CH_2OCOMe), 4.36 (1 H, dd, *J* 9.9, 1.2, one of CH_2OCOMe); *m/z* (EI) 329 (M^+ + 1, 7%), 255 (30), 147 (17), 130 (7), 115 (47), 99 (37), 85 (36), 69 (51), 57 (62), 43 (100) (Found: C, 69.4; H, 11.2. Calc. for $C_{19}H_{36}O_4$: C, 69.51; H, 10.98%). Enantiomeric excess was found to be >86% as determined by ^{1}H NMR spectroscopy using Eu(hfc)$_3$ shift reagent in $CDCl_3$, and by comparison with analogous spectra of the corresponding racemic acetate.

(−)-(2*S*,3*R*)-3-Tridecyloxymethyloxiran-2-ylmethyl 4-methylbenzenesulfonate

A procedure similar to (−)-(2*S*,3*R*)-3-propyloxiran-2-ylmethyl 4-methylbenzenesulfonate using (−)-(2*S*,3*R*)-3-tridecyloxymethyloxirane-2-methanol (1.10 g, 3.85 mmol), toluene-*p*-sulfonyl chloride (0.88 g, 4.62 mmol) and pyridine (14 cm^3) gave the crude product which was purified by column chromatography on flash silica (eluent 2:1 light petroleum–ethyl acetate) to give (2*S*,3*R*)-3-tridecyloxymethyloxiran-2-ylmethyl 4-methylbenzenesulfonate (1.18 g, 2.68 mmol, 70%) as an oil: $[\alpha]_D^{20}$ −7.79 (*c* 1.20 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 0.87 (3 H, t, *J* 6.6, CH_3), 1.23–1.28 (20 H, m, $[CH_2]_{10}CH_3$), 1.50–1.53 (2 H, m, $CH_2[CH_2]_{10}CH_3$), 2.44 (3 H, s, Ar-CH_3), 3.17–3.23 (2 H, m, H-2, H-3), 3.35–3.42 (2 H, m, $CH_2[CH_2]_{11}CH_3$), 3.45 (1 H, dd, *J* 11.5, 5.6, one of $CH_2O[CH_2]_{12}CH_3$), 3.58 (1 H, dd, *J* 11.5, 4.0, one of $CH_2O[CH_2]_{12}CH_3$), 4.11 (1 H, dd, *J* 11.4, 6.6, one of CH_2OTs), 4.26 (1 H, dd, *J* 11.4, 3.9, one of CH_2OTs), 7.34 (2 H, d, *J* 8.4, Ar-H), 7.79 (2 H, d, *J* 8.4, Ar-H); δ_C(75 MHz; $CDCl_3$) 14.08 (CH_3), 21.53 (Ar-CH_3), 22.64, 26.00, 29.31–29.61 (8 C), 31.87, 52.65 (C-2 or C-3), 54.77 (C-2 or C-3), 67.92, 68.27, 71.73, 127.90 (2 C, Ar), 129.85 (2 C, Ar), 132.70, 145.02; ν_{max}(thin film)/cm^{-1} 2900 (s), 2830 (m), 1630 (w), 1580 (m), 1440 (s), 1350 (s), 1160 (s), 1090 (s), 950 (s), 800 (s), 770 (m), 740 (m), 645 (s); *m/z* (FAB) 441 (M^+ + 1, 4%), 423 (20), 327 (6), 277 (12), 259 (5), 241 (7), 173 (19), 155 (56), 139 (24), 105 (22), 87 (94), 69 (100) (Found: M^+, 440.261. Calc. for $C_{24}H_{40}SO_5$: *M*, 440.260).

(+)-(2*S*,3*R*)-1-(*N*,*N*-Diallylamino)-2,3-epoxy-4-tridecyloxybutane 28

A procedure similar to (−)-(2*S*,3*R*)-1-(*N*,*N*-diallylamino)-2,3–epoxyhexane using (2*S*,3*R*)-3-tridecyloxymethyloxiran-2-ylmethyl 4-methylbenzenesulfonate (1.00 g, 2.27 mmol), potassium iodide (0.38 g, 2.27 mmol), DMF (11 cm^3) and diallylamine (0.44 g, 0.56 cm^3, 4.55 mmol) gave the crude product which was purified by column chromatography on flash silica (2:1 light petroleum–ethyl acetate) to give (+)-(2*S*,3*R*)-1-(*N*,*N*-diallylamino)-2,3-epoxy-4-tridecyloxybutane (0.67 g, 1.84 mmol, 81%) as a yellow oil; $[\alpha]_D^{20}$ +4.0 (*c* 0.80 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 0.88 (3 H, t, *J* 6.6, CH_3), 1.25–1.35 (20 H, m, $[CH_2]_{10}CH_3$), 1.54–1.59 (2 H, m, $CH_2[CH_2]_{10}CH_3$), 2.45 [1 H, dd, *J* 13.9, 6.4, one of $CH_2N(allyl)_2$], 2.79 [1 H, dd, *J* 13.9, 3.3, one of $CH_2N(allyl)_2$], 3.08 (2 H, dd, *J* 14.0, 6.8, 2 × allylic C*H*H), 3.12–3.17 (2 H, m, 2-H, 3-H), 3.26 (2 H, dd, *J* 14.0, 6.1, 2 × allylic C*H*H), 3.23–3.55 (3 H, m, $CH_2[CH_2]_{11}CH_3$ and one of $CH_2O[CH_2]_{12}CH_3$), 3.63 (1 H, dd, *J* 11.1, 3.6, one of $CH_2O[CH_2]_{12}CH_3$), 5.14–5.22 (4 H, m, $CH{=}CH_2$ × 2), 5.80–5.90 (2 H, m, C*H*=CH_2 × 2); δ_C(75 MHz; $CDCl_3$) 14.12 (CH_3), 22.68, 26.11, 29.35–29.66 (8 C), 31.91, 51.58, 54.33 (C-2 or C-3), 54.75 (C-2 or C-3), 57.21 (2 C, $CH_2CH{=}CH_2$ × 2), 68.80, 71.60, 117.83 (2 C, $CH{=}CH_2$ × 2), 135.27 (2 C, $CH{=}CH_2$ × 2); ν_{max}(thin film)/cm^{-1} 2900 (s), 2860 (m), 2820 (m), 1720 (m), 1625 (m), 1450 (s), 1355 (w), 1335 (w), 1245 (w), 1100 (s), 980 (m), 900 (s), 830 (m); *m/z* (EI) 364 (M^+ − 1, 12%), 338 (16), 324 (7), 182 (5), 166 (14), 152 (6), 110 (100), 70 (16), 57 (13) (Found: M^+, 365.328. Calc. for $C_{23}H_{43}NO_2$: *M*, 365.329).

(+)-(2*R*,3*R*)-3-(*N*,*N*-Diallylamino)-4-morpholino-1-tridecyloxybutan-2-ol 29

To a solution of (+)-(2*S*,3*R*)-1-(*N*,*N*-diallylamino)-2,3-epoxy-4-tridecyloxybutane (0.28 g, 0.77 mmol) in dichloromethane (7 cm^3) was added trimethylsilyl trifluoromethanesulfonate (0.20 g, 0.18 cm^3, 0.92 mmol) under nitrogen at −78 °C *via* syringe. After stirring for 10 min, morpholine (0.13 g, 0.13 cm^3, 1.53 mmol) was added. The reaction mixture was allowed to warm to room temperature and stirred for 5 days. Potassium carbonate (1.0 g, 7.25 mmol) and methanol (10 cm^3) were added and the mixture was stirred for 8 h. The solvents were removed and water (15 cm^3) and dichloromethane (15 cm^3) were added. The organic layer was then separated and aqueous layer was extracted with dichloromethane (3 × 10 cm^3), the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed *in vacuo* and the crude product was purified by column chromatography on flash silica (2:1 light petroleum–ethyl acetate) to give (2*R*,3*R*)-3-(*N*,*N*-diallylamino)-4-morpholino-1-tridecyloxybutan-2-ol (0.21 g, 0.47 mmol, 61%) as a colourless oil; $[\alpha]_D^{20}$ +17.7 (*c* 1.33 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 0.87 (3 H, t, *J* 6.6, CH_3), 1.24 (20 H, br s, $[CH_2]_{10}CH_3$), 1.53–1.57 (2 H, m, $CH_2[CH_2]_{10}CH_3$), 2.29 (1 H, dd, *J* 13.0, 6.0, 4′-C*H*H), 2.42 (4 H, br s, morpholine 3-CH_2, 5-CH_2), 2.54 (1 H, dd, *J* 13.0, 7.1, 4′-C*H*H), 2.98–3.04 [1 H, m, C*H*N(allyl)$_2$], 3.13 (2 H, dd, *J* 14.0, 8.2, 2 × allylic C*H*H), 3.34–3.50 (6 H, m, 2 × allylic C*H*H, $CH_2[CH_2]_{11}CH_3$, C*H*OH and one of $CH_2O[CH_2]_{12}CH_3$), 3.65–3.69 (5 H, m, morpholine 2-CH_2, 6-CH_2, one of $CH_2O[CH_2]_{12}CH_3$), 5.10–5.17 (4 H, m, $CH{=}CH_2$ x 2), 5.74–5.84 (2 H, m, C*H*=CH_2 × 2); δ_C(75 MHz; $CDCl_3$) 14.11, 22.68, 26.23, 29.34–29.78 (8 C), 31.90, 53.22, 54.12, 55.63, 56.40, 67.07, 69.74, 71.74, 72.87, 117.17, 136.76; ν_{max}(thin film)/cm^{-1} 3500–3250 (s, br), 2900 (s), 2820 (s), 1620 (s), 1440 (s), 1400 (m), 1360 (w), 1290 (m), 1260 (w), 1100 (s), 990 (m), 900 (s), 850 (m), 740 (m); *m/z* (EI) 451 (M^+ − 1, 22%), 423 (42), 411 (61), 352 (100), 110 (17), 100 (33), 71 (8), 57 (17) (Found: M^+, 452.397. Calc. for $C_{27}H_{52}N_2O_3$: *M*, 452.398).

(−)-(2*R*,3*R*)-3-Palmitoylamino-4-morpholino-1-tridecyloxybutan-2-ol 27[42,14b]

(2*R*,3*R*)-3-(*N*,*N*-Diallylamino)-4-morpholino-1-tridecyloxybutan-2-ol (0.34 g, 0.80 mmol), methanesulfonic acid (0.15 g, 1.59 mmol), 10% palladium on charcoal (0.11 g) and water (10 cm^3) were added to a two-necked round-bottomed flask fitted with a condenser. The mixture was heated under reflux

and a slow stream of N_2 passed through the solution to aid removal of propionaldehyde. This was continued for 12 h, with additional water being gradually added to keep the volume at approximately 10 cm^3. The reaction was then allowed to cool, neutralised (Na_2CO_3 aq.) and extracted with CH_2Cl_2 (3 × 10 ml). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude product was used in the next step without further purification. The crude (2*R*,3*R*)-3-amino-4-morpholino-1-tridecyloxybutan-2-ol (0.23 g, *ca.* 0.62 mmol) was dissolved in pyridine (10 cm^3) and *p*-nitrophenyl palmitate (0.30 g, 0.80 mmol) added. After 12 h at room temp., the reaction mixture was concentrated *in vacuo*, and the product isolated by chromatography (SiO_2, EtOAc eluent) to give (−)-(2*R*,3*R*)-3-palmitoylamino-4-morpholino-1-tridecyloxybutan-2-ol **27** (0.24 g, 0.39 mmol, 52% from **29**) as a pale yellow foam; $[\alpha]_D^{20}$ −2.14 (*c* 1.12 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 0.88 (6 H, t, *J* 6.7, 2 × CH_3), 1.26 (44 H, br s, $[CH_2]_{12}CH_3$ and $[CH_2]_{10}CH_3$), 1.53–1.62 (4 H, m, CH_2CH_2O and CH_2CH_2C=O), 2.15 (2 H, t, *J* 7.2, CH_2C=O), 2.47–2.59 (4 H, m, morpholine 3-CH_2, 5-CH_2), 2.55 (1 H, dd, *J* 12.7, 6.0, one of acyclic CH_2N), 2.63 (1 H, dd, *J* 12.7, 8.0, one of acyclic CH_2N), 3.40–3.49 (4 H, m, 2 × acyclic CH_2O), 3.66 (4 H, t, *J* 4.6, morpholine 2-CH_2, 6-CH_2), 4.01 (1 H, dt, *J* 2.3, 6.0, C*H*OH), 4.15–4.19 (1 H, m, C*H*NH), 6.16 (1 H, d, *J* 8.3, NH); δ_C(75 MHz; $CDCl_3$) 14.09 (2 × CH_3), 22.68 (2 × CH_2), 25.77 (CH_2), 26.18 (CH_2), 29.30 (2 × CH_2), 29.35 (3 × CH_2), 29.52 (2 × CH_2), 29.68 (12 × CH_2), 31.92 (CH_2CH_2O), 36.89 (CH_2C=O), 47.32 (*C*HNH), 54.17 (morpholine 3-CH_2, 5-CH_2), 59.68 (acyclic CH_2N), 66.96 (morpholine 2-CH_2, 6-CH_2), 70.37 (CHOH), 71.80 (acyclic CH_2O), 72.58 (acyclic CH_2O), 172.92 (C=O); ν_{max}($CHCl_3$)/cm^{-1} 3500–2200 (w, br OH), 3400 (w, NH), 2980 (m), 2900 (s), 2820 (s), 1645 (s, C=O), 1575 (w), 1490 (s), 1450 (s), 1330 (m), 1200 (m), 1100 (s), 1000 (w), 900 (w), 860 (w); *m/z* (EI) 609 ($M^+ - 1$), 591 ($M^+ - H_2O - 1$), 427 ($M^+ - C_{13}H_{27}$), 397 ($M^+ - CH_2O$-$[CH_2]_{13}H_{27}$), 142, 100 (morpholino group) (Found: C, 72.45; H, 12.40. Calc. for $C_{37}H_{74}N_2O_4$: C, 72.73; H, 12.21%).

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