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Lewis Acid Induced Rearrangement of 2,3-Epoxy sulfides; Regiospecific Trapping of Thiiranium Ion Intermediates with Nitrogen Heterocycles and Amides. Use of Imines as Nucleophilic Equivalents for the Selective Monoalkylation of Primary Amines.

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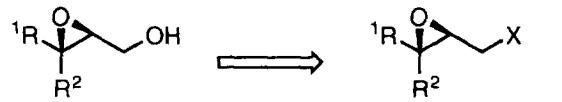
Abstract: The Lewis acid induced conversion of 2,3-epoxy sulfides into the corresponding 3-trimethylsilyloxy-1,2-thiiranium ions is described. Such intermediates react with silylated nitrogen heterocycles and amides regiospecifically to form 1-substituted-3-hydroxy-2-thioethers in good to moderate yields with full stereochemical control. Exclusive N-alkylation is observed. When simple primary amines are used as nucleophiles, only products of polyalkylation are isolated. However, imines can be effectively used as the nucleophilic equivalent of a primary amine, the initially formed iminium ions being readily hydrolysed by aqueous base to liberate a secondary amine, the product of overall selective monoalkylation of a primary amine.

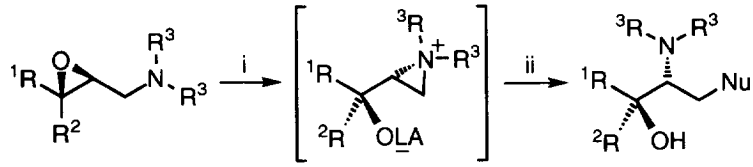
The Sharpless asymmetric epoxidation is one of the most useful asymmetric reactions available to the synthetic chemist.[1] In particular, the generality of the reaction allows for the preparation of a wide variety of homochiral 2,3-epoxy alcohols which are extremely useful synthetic intermediates.[2] 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**. These new systems represent new, readily available, optically active building block for use in synthesis, which have a high degree of functionality, and considerable potential for synthetic manipulation.[3,4]



1 **2**, X = NR^3_2, SR^3, SeR^3, PR^3_2

We have recently reported that 2,3-epoxy amines, *e.g.* **2**, **X = NBn$_2$**, undergo a highly efficient rearrangement to the corresponding 3-trimethylsilyloxy-1,2-aziridinium salts (equation 1) which can be trapped regiospecifically with nucleophiles at C-1 to form homochiral aminoalcohols.[5] This methodology has been recently extended to allow the use of amino acid ester based nucleophiles.[6] We have also studied in detail, the corresponding 2,3-epoxy sulfides **3**, and have recently reported a detailed study on the chemistry of the derived sulfoxides and sulfones, and shown how these useful synthetic intermediates can be transformed into 2,3-dihydroxy sulfoxides and E-γ-hydroxy-α,β-unsaturated sulfoxides and sulfones which are themselves useful and

interesting synthetic intermediates.[3] We have also reported that 2,3-epoxy sulfides undergo an analogous Lewis acid induced rearrangement to that of the amine system (*vide supra*) to give the corresponding thiiranium ion (episulphonium ion) (equation 2) which can be trapped regiospecifically by suitable nucleophiles to form homochiral 1-substituted-3-hydroxy-2-thioethers.[7]



Reagents and conditions: i, Lewis acid (LA); ii, Nucleophile (Nu)

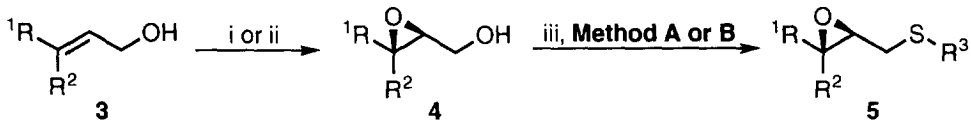
Thiiranium ions are interesting[8] and synthetically useful intermediates.[9] Their formation from β-hydroxy sulfides has been investigated by a number of groups, in particular Warren[10] and others,[11] however the use of epoxides for this type of reaction has not been reported to any significant degree.[12] This paper describes our work in this area in detail, and in particular, the nucleophilic trapping of the thiiranium ions generated *in situ* from 2,3-epoxy sulfides, with silylated nitrogen heterocycles, and amides, and also imines, which allow for overall selective monoalkylation of primary amines.[7]

Synthesis of 2,3-epoxy sulfides substrates.

We chose to study a range of 2,3-epoxy sulfide substrates to investigate the effects of epoxide geometry and sulfur substitution in order to gain a better understanding of the factors controlling the generation and reactivity of thiiranium ions. For our initial studies we chose the previously reported S-phenyl (5a) and S-methyl (5b) *trans*-2,3-epoxy sulfides,[3] the novel S-phenyl (5c) and S-methyl (5d) *cis*-2,3-epoxy sulfides and the S-benzyl (5e) and S-benzyloxypropyl (5f) *trans*-2,3-epoxy sulfides as representative substrates. The methyl and benzyl systems were of particular importance because they had the potential for deprotection to give the corresponding thiols, which was required as one of our long-term goals.[13,14] The phenyl group of (5a) and (5c) could be expected to moderate the reactivity of the thiiranium ion intermediate by delocalisation of the positive charge on the benzene ring. The benzyloxypropyl system (5f) provided a means to investigate the possibility of additional stabilisation of the thiiranium ion intermediate by coordination of the ether oxygen to the sulfonium sulfur atom (*vide infra*).[15] The *cis*- and *trans*-epoxides could be used to investigate the stereoselectivity of thiiranium ion formation, forming diastereomeric products after nucleophilic trapping, potentially allowing full control of the stereochemical configuration at both the chiral centres in the final product. Although the 2,3-epoxy sulfide substrates were mainly used as their racemates, one optically active system (5c) was investigated, firstly to monitor stereochemical integrity throughout the reaction sequence, but also because the required epoxy alcohol precursor could also only be obtained in low yield by racemic epoxidation using $VO(acac)_2$ catalysis,[16] but gave good yields using the asymmetric epoxidation system.[1]

The 2,3-epoxy sulfides were prepared by two routes (table 1) from the racemic or optically active 2,3-epoxy alcohol, either using a disulfide and tributyl phosphine (method A),[17] or by conversion of the alcohol into the *p*-toluenesulfonate ester and selective nucleophilic displacement in the presence of the epoxide (method B). The S-phenyl thioethers were readily prepared by method A, which could also be used for the S-methyl *trans*-

2,3-epoxy sulfides. However, in the case of the S-methyl *cis*-epoxyalcohol (entry 5), only a very low yield could be obtained using this method. Fortunately, method B gave a very good yield in this case, and was thus the method of choice for preparing the remaining dialkyl thioethers.



3 4 5

Reagents and conditions: i, Bu^tOOH, $VO(acac)_2$, CH_2Cl_2, $R^1 = {}^nPr$, $R^2 = H$, 85%; $R^1 = H$, $R^2 = {}^nPr$, <10%, ii, Bu^tOOH, $Ti(O^iPr)_4$, L-(+)-DET, CH_2Cl_2, $R^1 = {}^nPr$, $R^2 = H$, 86%; $R^1 = H$, $R^2 = {}^nPr$, 72%; iii, **Method A:** R^3SSR^3, PBu_3; **Method B:** TsCl, pyridine; R^3SNa, DMF

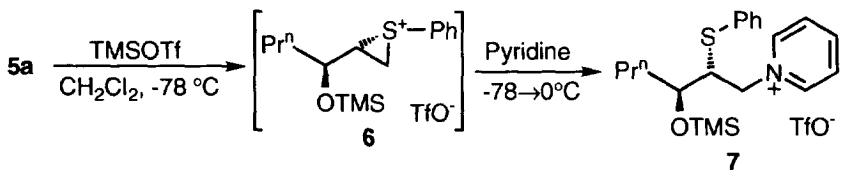
Entry	Compound	R^1	R^2	R^3	Method	Yield (%)
1	**5a**	^nPr	H	Ph	A	74
2	**5b**	^nPr	H	Me	A	54
3	**5c**	H	^nPr	Ph	A	81
4	**5d**	H	^nPr	Me	A	25
5	**5d**	H	^nPr	Me	B	82
6	**5e**	^nPr	H	Bn	B	75
7	**5f**	^nPr	H	$(CH_2)_3OBn$	B	49

Table 1: Synthesis of 2,3-epoxy sulfide substrates

Generation of thiiranium ions from 2,3-epoxy sulfides.

The conversion shown in equations 1 and 2 are related to the known Payne rearrangement-nucleophilic trapping procedure of 2,3-epoxy alcohols[18,19] which is particularly useful if selective nucleophilic trapping of the more reactive intermediate in an equilibrium mixture, can be achieved.[19] In this case, our original goal was to investigate the possibility of a similar process occurring with a 2,3-epoxy sulfide, but fundamental differences were likely. The generation of a thiiranium ion from a 2,3-epoxy sulfide is not necessarily an equilibrium process like the Payne rearrangement as it is no longer a true isomerisation. It may thus be possible to effectively convert all the starting material into the reactive intermediate, which can subsequently be trapped by a suitable nucleophile. This would have significant advantages over the equilibrium process. We thus initially began to investigate the generation of thiiranium ions under Lewis acidic conditions.

A number of thiiranium ions have been isolated and characterised.[20] We initially attempted to generate and isolate thiiranium ions generated by treatment of the S-phenyl *trans*-2,3-epoxy sulfide **5a** with a Lewis acid ($BF_3{\cdot}OEt_2$ or TMSOTf) in CH_2Cl_2 at -78 °C then warming to rt (scheme 1).



Scheme 1

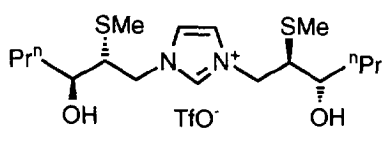
TLC showed a rapid disappearance of starting material, but no characterisable products could be seen by ^{1}H NMR. We believed that decomposition of the thiiranium ion/Lewis acid complex may be occurring on warming due to extraneous acid in the reaction medium, and therefore added a base (pyridine) whilst still at -78 °C (scheme 1). In this case, after warming and removal of solvent *in vacuo*, a new compound was formed very cleanly as rather unstable colouress needles, but rather than being a thiiranium ion, was identified as the pyridinium triflate **7**, isolated in near quantitative yield. This was a very significant result for three reasons. Firstly, the thiophenyl group had cleanly undergone a 1,2-migration - an observation often used to imply the intermediacy of a thiiranium ion.[10] This was good evidence that our initial concept for thiiranium ion generation was sound, but that the thiiranium ion intermediate was too unstable to be isolated. Frequently, thiiranium ions are postulated as reactive intermediates, but are not actually isolated.[9,10,11] The second important observation was that the postulated thiiranium ion intermediate had been opened exclusively at C-1 by the nucleophile, no other products being observed in the crude product mixture - this was a nice clean regioselective reaction. Finally, the pyridinium salt **7** was a single diastereoisomer by ^{1}H NMR, which implied that the rearrangement to form the thiiranium ion was a stereospecific process, and that thiiranium ions are sufficiently configurationally stable to be useful in asymmetric synthesis.[21] This also had significant implications for other methods of enantioselective thiiranium ion generation currently under development in our group.[22] All of these factors convinced us that we had the basis for a very powerful method for the synthesis of functionalised β-hydroxy sulfides with full regio- and stereochemical control.

Investigations into the nucleophilic trapping of thiiranium ions with sp^2 hybridised nitrogen nucleophiles.

We thus began to investigate further the range of nucleophiles which could be used, and the effect of varying the structure of the 2,3-epoxy sulfide substrate. Addition of a variety of nitrogen nucleophiles to the thiiranium ions formed *in situ*, warming to 0°C and stirring for up to 3 days gives the corresponding O-trimethylsilyl ethers which can be readily deprotected (K_2CO_3, MeOH) (table 2).

Because pyridine had worked so well in our preliminary studies, we originally chose to investigate other sp^2 nitrogen systems, and in keeping with a general interest in the synthesis of molecules with possible biological activity, the use of silylated precursors to uracils,[23] imidazoles,[24] and amides were studied.[25] In general, yields ranged from low to very good. They refer to pure products after chromatography, and are overall yields for the 3 step sequence of thiiranium ion generation, nucleophilic trapping and deprotection. In all cases the products are single diastereoisomers and regioisomers as determined by ^{13}C NMR. Importantly, when homochiral 2,3-epoxy sulphide substrates are used, the products retain their optical activity (entries 5 and 13).

The 2-pyridones and uracils gave best yields, and the simple (S-Me, S-Ph) *trans*-2,3-epoxy sulfides were better substrates than the *cis*-isomers. The benzyloxypropyl system gave a low yield, and we propose that this may be due to stabilisation of the thiiranium ion by coordination to the sulfonium sulfur (figure 1) although we have so far been unable to confirm this directly and we are currently investigating this effect further. This is related to other known systems where thiiranium ions are stabilised by adjacent coordinating substituents, which render them much less reactive than would be otherwise expected (*cf.* figure 2).[15]



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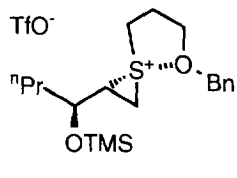


Figure 1

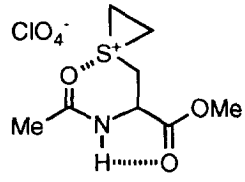
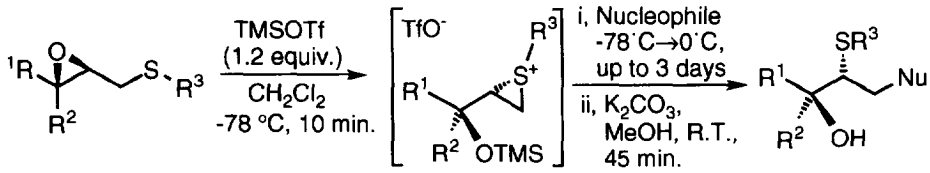
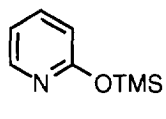
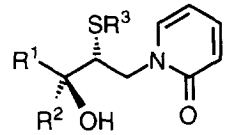
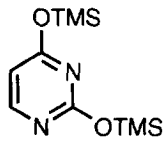
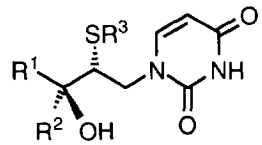
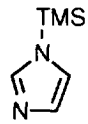
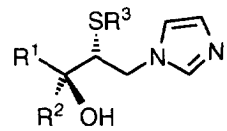
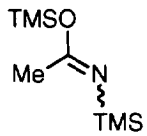
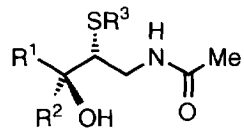
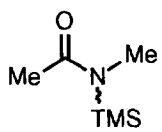
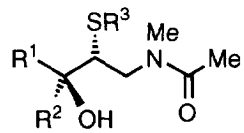


Figure 2



Entry[a]	Substrate	Nucleophile	Product	Yield (%)
1	**5a**			81
2	**5b**			85
3	**5a**			75
4	**5b**			81
5	**5c**[b]			55[c]
6	**5d**			68
7	**5e**			53
8	**5f**			20
9	**5a**			39 (83[e])
10	**5b**			33
11	**5a**			58
12	**5b**			54
13	**5c**[b]			40[d]
14	**5d**			44
15	**5e**			51
16	**5a**			55
17	**5b**			44

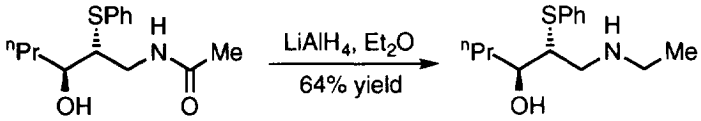
[a]All compounds used as racemates unless otherwise stated; [b]Optically active (>95% e.e.) 2,3-epoxysulphide used; [c]$[\alpha]_D^{25}$+36.6 (*c* 1.18, EtOH); [d]$[\alpha]_D^{25}$+47.6 (*c* 0.97, EtOH); [e]Yield based on recovered starting material.

Table 2: Results of thiiranium ion trapping experiments with silylated nitrogen heterocycles and amide nucleophiles

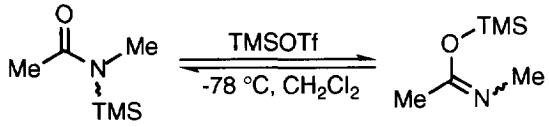
The imidazole system showed only low reactivity. With the S-phenyl thiiranium ion, a considerable amount of starting material could be recovered, however in the case of the S-methyl system, no starting material was observed, only a moderate yield of products was obtained, and significant amounts (30-40%) of a

byproduct, tentatively assigned as the *bis*-alkylated imidazolium salt **8** was observed in the crude ^1H NMR but could not be isolated in a pure form. Thus it would appear that, at least in this case, the S-alkyl thiiranium ions are more reactive than the S-phenyl systems.

In the case of the amide nucleophiles (entries 11 to 17), both gave moderate yields of the desired products. Clean N-alkylation was observed. This was proved unambiguously in one case (entry 11) by reduction of the amide product with $LiAlH_4$ (scheme 2). The product obtained was clearly the N-ethylamine. Trimethylsilylacetamide is reported to exist as the N-silylated isomer,[25] although this would be expected to undergo O-alkylation. However it is likely that under the reaction conditions (TMSOTf), silyl migration can readily occur to give the O-trimethylsilylacetamide (scheme 3), which would be expected to undergo the observed N-alkylation.



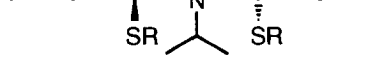
Scheme 2



Scheme 3

Use of secondary and primary amine nucleophile equivalents.

Although the systems which had worked well so far were of use, we also needed to extend the chemistry for the introduction of secondary and primary amines. In particular, as part of a general programme aimed at the synthesis of novel aminopeptidase inhibitors, we needed a system which allowed the use of α-aminoacid ester nucleophiles.[6,7c] The relative success of silylated nucleophiles in our previous work led us to initially consider the use of N-trimethylsilyl amines[26] as nucleophilic equivalents of secondary amines in the reaction (table 3). As can be seen these gave moderate yields of the desired products, particularly if BF_3•OEt_2 is used as Lewis acid rather than TMSOTf. These yields were generally acceptable, however the real problems began when we investigated the use of primary amines. Isopropylamine was chosen initially as a simple model system for an amino acid ester, however all attempts at reacting isopropylamine with one of our thiiranium ions resulted in isolation of the *bis*-alkylated compound **9** as the sole characterisable product. Use of a large excess of nucleophile, and modification of reaction conditions, failed to improve the selectivity of the reaction. The use of silylated primary amines, such as the stabase derivatives of isopropylamine, Ala(OMe) and Leu(OMe)[27] and other silylated nucleophiles such as $(Me_3Si)_3N$ and $(Me_3Si)_2NMe$ in some cases gave monoalkylation products but only in <20% yield.



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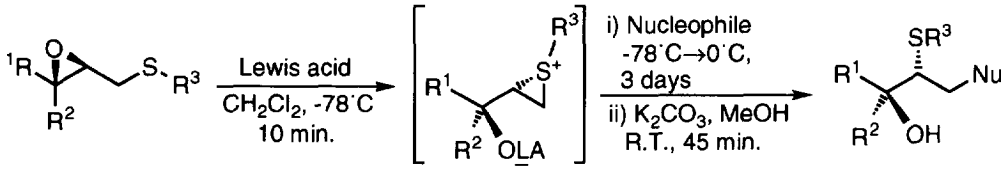
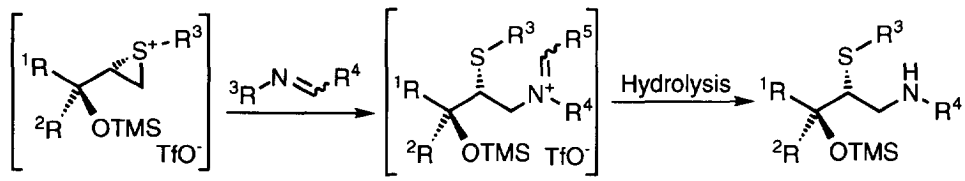
We thus needed to develop a system which would efficiently trap the thiiranium ion intermediates with effective monoalkylation, and allow ready conversion to the final secondary amine product in good yield. The success of some of the sp^2 nitrogen nucleophiles (*e.g.* 2-trimethylsilyloxypyridine) in the earlier work led us to consider the use of imines as synthetic equivalents for primary amines in this reaction. They would be expected to undergo only monoalkylation to give an iminium ion, which on work-up would be readily hydrolysed to the desired secondary amine product (scheme 4). Related procedures have previously been reported for the preparation of secondary amines using dimethyl sulfate and alkyl halides as alkylating agents.[28]



Entry[a]	Substrate	Nucleophile	Lewis acid	Product	Yield (%)
1	**5a**		TMSOTf		23
2	**5a**	N–TMS	BF_3•OEt_2		40
3	**5b**		TMSOTf		37
4	**5b**		BF_3•OEt_2		47
5	**5b**	O N–TMS	BF_3•OEt_2		44
6	**5a**	N–TMS	BF_3•OEt_2		33
7	**5b**		BF_3•OEt_2		37

[a]All compounds used as racemates.

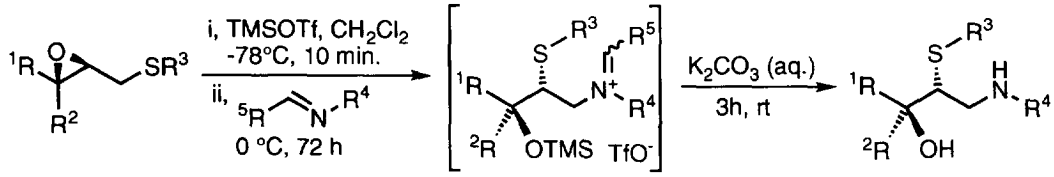
Table 3: Results of thiiranium ion trapping experiments with N-trimethylsilyl amines.



Scheme 4

A number of simple imine derivatives were prepared including benzaldehyde isopropylimine,[29] anisaldehyde isopropylimine,[30] and acetaldehyde isopropylimine,[31] and their efficiency as thiiranium ion trapping agents investigated using our newly developed thiiranium ion system (table 4, entries 1-3). The initially formed iminium triflates could be isolated, but were generally hydrolysed using aqueous K_2CO_3 during work-up, which

also served to deprotect the trimethylsilyl ether. Note that yields are for the 4 step reaction sequence (*viz.* thiiranium ion generation, iminium ion formation, hydrolysis, and deprotection) and purification.



Entry	Substrate	H_2N-R^4	R^5	Yield
1	**5b**	^{i}PrNH$_2$	C_6H_5	37[a]
2	**5b**	^{i}PrNH$_2$	(4-MeO)C_6H_4	63[a]
3	**5b**	^{i}PrNH$_2$	Me	70[a]
4	**5c**	^{i}PrNH$_2$	(4-MeO)C_6H_4	57
5	**5c**	PhNH$_2$	(4-MeO)C_6H_4	66[b]
6	**5c**	BnNH$_2$	(4-MeO)C_6H_4	46

[a]Racemic 2,3-epoxy sulfide used; [b]Isolated as O-trimethylsilyl ether

Table 4: Use of imines as synthetic equivalents for the selective monoalkylation of primary amines.

It can be seen that the *p*-anisaldehyde imine (entry 2) and acetaldehyde imine (entry 3) were of similar efficiency, however the instability of the latter meant that for reproducibility the *p*-anisaldehyde imines were preferred. The acetaldehyde-derived imines were generally used without purification immediately after preparation, and tended to give coloured products (this could be suppressed by addition of ^{i}PrNH$_2$ prior to work-up) whereas the anisaldehyde imines could be purified prior to use and generally gave cleaner products. For this reason the anisaldehyde imines were chosen for further investigation into the effect of the nature of the amine structure on the reaction. The benzaldehyde imine was clearly inferior in this reaction.

Thus anisaldehyde isopropylimine, anisaldehyde phenylimine,[32] and anisaldehyde benzylimine[33] were all reacted with the same 2,3-epoxy sulfide substrate. The reactions generally proceeded with similar efficiency. One interesting point to note is the unusual stability of the O-trimethylsilyl ether obtained by reaction of the phenylimine, which allowed for its isolation without *in situ* deprotection under the conditions required for imine hydrolysis. Thus use of this procedure gives the required secondary amines, which are the desired products of overall selective monoalkylation of primary amines by the thiiranium ion.

Summary

In summary, this new powerful methodology provides access to a range of functionalised 1-amino-3-hydroxy-2-thioethers with full control of absolute and relative stereochemistry. Use of appropriate silylated precursors allows the introduction of pyridone, uracil, imidazole and amide and secondary amine substituents. Use of primary amine nucleophiles results in polyalkylation, however imines can be used as synthetic equivalents for primary amines in reactions with thiiranium ions, allowing clean monoalkylation, with the initially formed iminium ions being readily hydrolysed to give the desired product secondary amines. Further investigations into the versatility of this reaction, and the nature of the reactive intermediates involved, are currently underway in our laboratories.

Experimental Section

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 deuterated 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 and calibrated using a solution of camphor in ethanol of known rotation, $[\alpha]_D^{20}$ +44.1° (*c* 10, ethanol). 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[34].

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 mm Hg.

Solvents were purified prior to use by established procedures[35] and other reagents used as received. Petroleum ether refers to petroleum ether (b.p. 40-60°C) unless otherwise stated. Methyl disulfide was purified prior to use by passing through a short column of silica gel. *p*-Toluene sulfonyl chloride was purified prior to use by recrystallisation from petroleum ether. Hexamethyldisilazane was purified prior to use by distillation. Trimethylsilyl trifluoromethanesulfonate was obtained from the Aldrich Chemical Company Ltd. and used immediately upon opening. Sodium methanethiolate was purchased from the Aldrich Chemical Company Ltd. 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-propyloxiranemethanol (**4a**)[1a,3], (-)-(2*S*,3*R*)-3-propyloxiranemethanol (**4b**)[36], (-)-2-[(phenylthio)methyl]-(2*R*,3*S*)-3-propyloxirane (**5a**)[3], (-)-2-[(methylthio)methyl]-(2*R*,3*S*)-3-propyloxirane (**5b**)[3], O-trimethylsilyl-2-pyridone[25], bis-*O*-trimethylsilyl-uracil[37], *N*-methyl-*N*-trimethylsilylacetamide[25], *N*-iso-propyl *p*-anisylidene imine[30], *N*-phenyl *p*-anisylidene imine[32], *N*-benzyl *p*-anisylidene imine[32], *N*-iso-propyl benzylidene imine[29], and *N*-iso-propyl *p*-acetylidene imine[30]. Enantiomeric excesses of epoxy alcohols (**4**) were determined by ^1H NMR using $Eu(hfc)_3$ on the corresponding acetate derivative.

Experimental details

(+)-2-[(Phenylthio)methyl]-(2R,3R)-3-propyloxirane (**5c**), (table 1, entry 3).

Phenyl disulfide (6.99g, 32.1mmol) was added to a solution of (-)-(2*S*,3*R*)-3-propyloxiranemethanol (**4b**) (2.48g, 21.4mmol) in DMF (12ml) with stirring at 0°C. Tri-*n*-butyl phosphine (7.98ml, 32.1mmol) was added dropwise by syringe. The reaction was allowed to warm to room temperature and stirred for 18h. It was then poured into water (250ml) and washed with petroleum ether (5 x 50ml). The combined organic portions were washed with 1M sodium hydroxide solution (2 x 50ml) and brine (50ml), then dried ($MgSO_4$) and filtered. Methyl iodide (2.67ml, 42.8mmol) was added and the mixture shaken for 5 min, filtered through a pad of celite and concentrated. Flash chromatography (silica, 200g, eluent 3% ethyl acetate / petroleum ether) gave *(+)-2-[(phenylthio)methyl]-(2R,3R)-3-propyloxirane* (**5c**) (3.61g, 17.3mmol, 81% yield) as a colourless oil: b.p. 100-104°C / 0.025mmHg; ^1H NMR (300 MHz, $CDCl_3$), δ 0.94 (t, J 7.1, 3H, CH_3CH_2), 1.30-1.58 (m, 4H, CH_2CH_2), 2.88-2.98 (m, 2H, CH_2SPh), 3.08-3.20 (m, 2H, CH-2 + CH-3), 7.17-7.33 (m, 3H, *o*-, *p*- Ar-H), 7.42 (d, J 7.2, 2H, *m*- Ar-H); IR (thin film) 3060 (m), 2980 (s), 2960 (s), 2885 (s), 1590 (s), 1485 (s), 1465 (s), 1440 (s), 1380 (m), 1260 (m), 1230 (m), 1090 (m), 1070 (m), 1025 (m), 965 (m), 875 (m), 820 (m), 740 (s), 695 (s); MS (EI) *m/e* 208 (m^+) (52), 165 (22), 137 (26), 123 (53), 110 (79), 109 (74), 99 (43), 71 (40), 65 (47), 57 (70), 55 (88), 51 (27), 45 (36), 43 (100), 41 (47), 39 (43), 32 (59); Analysis calculated for $C_{13}H_{18}O_4S$: C, 69.19; H,7.74; S, 15.39; found: C, 69.15; H, 7.90; S, 15.40, $[\alpha]_D^{20}$ +69.3° (*c* 1.38, ethanol).

(±)-2-[p-Toluenesulfonyloxymethyl]-(2S,3S*)-3-propyloxirane.*
p-Toluene-sulfonyl chloride (9.88g, 51.7mmol) was added to (±)-(2*S**,3*S**)-3-propyloxiranemethanol (**4a**) (5.00g, 43.1mmol) in pyridine (20ml) at 0°C, allowed to warm to room temperature and stirred overnight. The reaction mixture was then poured into 0.5M sulfuric acid (250ml) and washed with diethyl ether (3 x 100ml). The combined organic portions were dried ($MgSO_4$), filtered and concentrated. Flash chromatography (silica, 250g, eluent 10% ethyl acetate / petroleum ether) gave *(±)-2-[p-toluenesulfonyloxymethyl]-(2S*,3S*)-3-propyloxirane* (6.74g, 25.0mmol, 58% yield) as a colourless oil: ^{1}H NMR (300MHz, $CDCl_3$) δ 0.93 (t, J 6.9, 3H, C$\underline{H}_3$C$\underline{H}_2$), 1.37-1.50 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 2.46 (s, 3H, C$\underline{H}_3$Ar), 2.99 (apparent q, J 5.8, 1H, C$\underline{H}$-3), 3.16 (dt, J 6.5, 5.8, 1H, C$\underline{H}$-2), 4.08 (dd, J 11.3, 6.3, 1H, one of C$\underline{H}_2$-1), 4.18 (dd, J 11.3, 5.0, 1H, remaining C$\underline{H}_2$-1), 7.36, 7.82 (AB system, J 8.7, 4H, Ar$\underline{H}$); ^{13}C NMR (75MHz, $CDCl_3$) δ 13.45 (CH_3-6), 18.73 (CH_2-5), 21.24 (CH_3-Ar), 32.93 (CH_2-4), 54.16 (CH-3), 56.05 (CH-2), 70.15 (CH_2-1), 127.55 (CH-Ar), 129.65 (CH-Ar), 132.41 (CH-Ar), 144.80 (C-Ar); MS (EI) *m/e* 270 (M^+, 0.3), 227 (7), 155 (100), 91 (91), 65 (19), 55 (20), 41 (15); IR (thin film) 2960 (s), 2930 (m), 2870 (m), 1600 (m), 1450 (m), 1360 (s), 1190 (m), 1180 (m), 1110 (m), 960 (s), 900 (m), 810 (m), 790 (m), 665 (s); Analysis calculated for $C_{13}H_{18}O_4S$: C, 57.76; H, 6.71; S, 11.86; found: C, 57.45; H, 6.75; S, 11.75.

(-)-2-[p-Toluene-sulfonyloxymethyl]-(2S,3R)-3-propyloxirane.
Prepared by an analogous procedure from (-)-(2*S*,3*R*)-3-propyloxiranemethanol (**4b**) in 58% yield as a colourless oil: ^{1}H NMR (300MHz, $CDCl_3$) δ 0.93 (t, J 6.9, 3H, C$\underline{H}_3$C$\underline{H}_2$), 1.37-1.50 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 2.46 (s, 3H, C$\underline{H}_3$Ar), 2.99 (dt, J 6.2, 4.6, 1H, C$\underline{H}$-3), 3.16 (dt, J 6.2, 5.0, 1H, C$\underline{H}$-2), 4.08 (dd, J 11.3, 5.0, 1H, one of C$\underline{H}_2$-1), 4.18 (dd, J 11.3, 5.0, 1H, remaining C$\underline{H}_2$-1), 7.36 (d, J 8.7, 4H, 2 of Ar$\underline{H}$), 7.82 (d, J 8.7, 4H, remaining Ar$\underline{H}$); ^{13}C NMR (75MHz, $CDCl_3$) δ 13.54 (CH_3-6), 19.55 (CH_2-5), 21.36 (CH_3-Ar), 29.43 (CH_2-4), 52.68 (CH-3), 56.10 (CH-2),68.09 (CH_2-1), 127.77 (CH-Ar), 129.76 (CH-Ar), 132.39 (CH-Ar), 144.92 (C-Ar); MS (EI) *m/e* 271 (M^++1) (11), 253 (M^++ 1-H_2O), 227 (26), 173 (16), 155 (80), 139 (29), 107 (24), 99 (82), 97 (29), 91 (91), 81 (100), 65 (66), 55 (70), 43 (66); IR (thin film) 2965 (s), 2935 (m), 2875 (m), 1605 (m),1465 (m), 1365 (s), 1195 (s), 1185 (s), 1105 (m), 975 (s), 820 (s), 675 (s); Analysis calculated for $C_{13}H_{18}O_4S$: C, 57.76; H, 6.71; S, 11.86; found: C, 57.45; H, 6.75; S, 11.75; $[\alpha]_D^{20}$ -15.1° (*c* 1.46, ethanol).

(+)-2-[(Methylthio)methyl]-(2R,3R)-3-propyloxirane (**5d**), (table 1, entry 5).
A solution of sodium methanethiolate (3.89g, 55.6mmol) in DMF (10ml) was added by syringe to (-)-2-[*p*-toluene-sulfonyloxymethyl]-(2S,3R)-3-propyloxirane in DMF (10ml) at 0°C and stirred for 5 min. The reaction mixture was poured into water (500ml) and extracted with petroleum ether (5 x 50ml). The combined petroleum ether extracts were washed with aqueous sodium hydroxide solution (1M, 2 x 100ml) and brine (100ml), dried ($MgSO_4$), filtered and concentrated. Distillation under reduced pressure gave *(+)-2-[(methylthio)methyl]-(2R,3R)-3-propyloxirane* (**5d**) (2.21g, 15.1mmol, 82% yield) as a colourless oil: b.p.38-40°C / 0.04mmHg; ^{1}H NMR (300MHz, $CDCl_3$) δ 0.93 (t, J 7.1, 3H, C$\underline{H}_3$C$\underline{H}_2$), 1.42-1.63 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 2.22 (s, 3H, SC$\underline{H}_3$), 2.61 (dd, J 13.4, 6.3, 1H, one of C$\underline{H}_2$-1), 2.68 (dd, J 13.4, 6.1, 1H, remaining C$\underline{H}_2$-1), 2.98 (td, J 5.2, 4.3, 1H, C$\underline{H}$-3), 3.17 (td, J 6.2, 4.3, 1H, C$\underline{H}$-2); MS *m/e* 146 (M^+) (24), 107 (45), 103 (30), 75 (20), 61 (100), 57 (57), 55 (66), 43 (53), 41 (47); IR (thin film) 2960 (s), 2920 (s), 2840 (s), 1430 (s), 1380 (m), 1320 (w), 1265 (m), 1235 (m), 1260 (w), 1240 (w), 1090 (w), 990 (m), 960 (m), 880 (w), 860 (w), 820 (m), 760 (s) 700 (m); accurate mass (EI): calculated for $C_7H_{14}OS$ = 146.077; found 146.075; $[\alpha]_D^{20}$ +24.1° (*c* 1.11, ethanol).

(±)-2-[(Phenylmethylthio)methyl]-(2R,3S*)-3-propyloxirane* (**5e**), (table 1, entry 6).
Sodium metal (256mg, 11.1mmol) was added to benzyl thiol (1.1g, 8.89mmol) in dry diethyl ether (10ml) and stirred overnight. The solvent was removed and the precipitate dissolved in dimethylformamide (10ml) and decanted from the remaining sodium metal. (±)-2-[*p*-Toluenesulfonyloxymethyl]-(2*S**,3*S**)-3-propyloxirane (2.0g, 7.41mmol) was added and the mixture stirred at room temperature for 2 hours. The reaction mixture was poured into water (100ml) and extracted with petroleum ether (5 x 25ml). The combined extracts were dried ($MgSO_4$), filtered and concentrated. Flash chromatography (silica, 50g, eluent 3% ethyl acetate / petroleum ether) gave *(±)-2-[(phenylmethylthio)methyl]-(2R*,3S*)-3-propyloxirane* (**5e**) (1.23g, 5.56mmol, 75% yield) as a colourless oil: ^{1}H NMR (300MHz, $CDCl_3$) δ 0.94 (t, J 7.1, 3H, C$\underline{H}_3$C$\underline{H}_2$), 1.30-1.60 (m, 4H,

$C\underline{H}_2C\underline{H}_2$), 2.47 (dd, J 13.0, 5.4, 1H, one of $C\underline{H}_2$-1), 2.62 (dd, J 13.0, 5.4, 1H, remaining $C\underline{H}_2$-1), 2.67-2.74 (m, 1H, C<u>H</u>-3), 2.78-2.86 (m, 1H, C<u>H</u>-2), 3.80 (s, 3H, $C\underline{H}_2$Ph), 7.20-7.44 (m, Ar-<u>H</u>); MS (CI)*m/e* 223 (M^++1, 100); IR (thin film) 3061 (m),3028 (m), 2960 (s), 2931 (s) 2873 (m), 1495 (m), 1454 (s), 924 (m), 701 (s); accurate mass (CI): calculated for M^++1 $C_{13}H_{19}OS$ = 223.116; found 223.114.

(±)-2-(Phenylmethyl)oxypropylthiomethyl)-(2R,3S*)-3-propyloxirane* (**5 f**), (table 1, entry 7).

3-(Phenylmethyl)oxypropan-1-ol [38]

1,3-Propanediol (43.4ml, 0.6mol), benzaldehyde (51ml, 0.5mol), *p*-toluenesulfonic acid (0.5g) and toluene (500ml) were heated at reflux with azeotropic removal of water for 210 min. The mixture was allowed to cool, washed with aqueous sodium hydroxide (1M, 2 x 150ml), dried ($MgSO_4$), filtered and concentrated to give 2-phenyl-1,3-dioxane (95g, 0.58mol, 97% yield), used without further purification. Anhydrous aluminium chloride (16.3g, 0.122mol) was added portionwise to 50ml ether and the solution cooled to 0°C with stirring. Lithium aluminium hydride (1.22g, 32mmol) was added portionwise and stirring continued for 30 min. A solution of the crude 2-phenyl-1,3-dioxane (10g in 20ml diethyl ether) was added dropwise and the mixture stirred for 30 min, allowed to come to room temperature and stirred for a further 30 min. 10% aqueous sulfuric acid (100ml) was added dropwise over 30min with stirring. The aqueous layer was separated and washed with ether (3x20ml), then the ether layer was then combined with these washings, dried ($MgSO_4$) and concentrated to give 3-(phenylmethyl)oxypropan-1-ol (7.7g, 46mmol, 75% yield) as a colourless oil, used without further treatment: ^{1}H NMR (300MHz, $CDCl_3$) δ 1.82 (quintet, J 6.0, 2H, $C\underline{H}_2$-2), 2.73 (s, 1H, $CH_2O\underline{H}$), 3.61 (t, J 6.0, 2H, $C\underline{H}_2$-1), 3.71 (t, J 6.0, 2H, $C\underline{H}_2$-3), 4.50 (s, 2H, $C\underline{H}_2$Ar), 7.22-7.36 (m, 7H, Ar<u>H</u>).

3-(Phenylmethyl)oxypropan-1-(4'-methylphenyl)sulfonate

p-Toluenesulfonyl chloride (2.76g, 14.5mmol) in pyridine (5ml) was added dropwise to 3-benzyloxypropan-1-ol (2g, 12mmol) in pyridine (10ml) at-10°C and stirred for 1 h. An ice / water mixture (150ml) was added and the mixture extracted with ether (5x100ml). To the combined ethereal extracts were added petroleum ether (100ml) and the mixture then washed with 0.5M sulfuric acid (100ml). The aqueous layer was separated and extracted with diethyl ether / petroleum ether (1:1, 3x40ml). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated to give *3-(phenylmethyl)oxypropan-1-(4'-methylphenyl)sulfonate* (2.80g, 8.80mmol, 73% yield) as a colourless oil: ^{1}H NMR (300MHz, $CDCl_3$) δ 1.98 (quintet, J 6.0, 2H, $C\underline{H}_2$-2), 2.42 (s, 3H, $C\underline{H}_3$-Ar), 3.50 (t, J 6.0, 2H, $C\underline{H}_2$-3), 4.17 (t, J 6.0, 2H, $C\underline{H}_2$-1), 4.40 (s, 2H, $C\underline{H}_2$Ar), 7.22-7.33 (m, 7H, $C_6\underline{H}_5$ + 2 of $C_6\underline{H}_4$), 7.78 (part of AB system, J 8.1, 2H, remaining $C_6\underline{H}_4$); ^{13}C NMR (75MHz, $CDCl_3$) δ 21.38 (CH_3-Ar), 29.14 (CH_2-2), 65.46 (CH_2-3), 67.54 (CH_2-1), 72.78 (CH_2-Ph), 127.30 (CH-Ar), 127.39 (CH-Ar), 127.66 (CH-Ar), 128.15 (CH-Ar), 129.65 (CH-Ar), 132.86 (C-Ar), 137.95 (C-Ar), 144.54 (C-Ar); MS (EI), *m/e* 320 (M^+, 2), 214 (3), 172 (16), 147 (51), 107 (27), 91 (100), 79 (20), 65 (33), 51 (11); IR (thin film) 3040 (w), 2860 (m), 1600 (w), 1450 (m), 1350 (S), 1290 (w), 1240 (w), 1210 (w), 1170 (s), 1110 (s), 1095 (s), 1070 (m), 1040 (m), 1020 (w), 970 (m), 940 (s), 900 (w), 850 (m), 810 (s), 755 (s), 700 (s), 660 (s).

3-(Phenylmethyl)oxypropan-1-thiol

3-(Phenylmethyl)-oxypropan-1-(4'-methylphenyl)sulfonate (8.47g, 26.5mmol) was heated under reflux with potassium ethyl xanthate (6.35g, 39.7mmol) in acetone (50ml) for 30 min. The precipitate was removed by filtration and washed with acetone (2 x 20 ml). The combined acetone fractions were concentrated, redissolved in chloroform (200ml) and extracted with water (3 x 20ml). The aqueous extracts were combined and back-extracted with chloroform (25 ml). The chloroform extracts were combined, dried ($MgSO_4$), filtered and concentrated to give crude *S-3-(phenylmethyl)oxypropyl-O-ethylxanthate* used without further purification. The crude product was stirred with ethylene diamine (15.9g, 265mmol) for 3d at rt, poured onto ice / 10% sulfuric acid solution (80ml) and extracted with diethyl ether (3 x 15 ml). The ethereal extracts were combined, dried ($MgSO_4$), filtered and concentrated to give crude *3-(phenylmethyl)oxypropan-1-thiol* (4.35g, 23.9mmol, 90% yield) as a yellow oil, used without further purification: ^{1}H NMR (300MHz, $CDCl_3$) δ 1.91 (quintet, J 6.0, 2H, $C\underline{H}_2$-2), 2.65 (t, J 6.0, 2H, $C\underline{H}_2$-1), 3.57 (t, J 6.0, 2H, $C\underline{H}_2$-3), 4.50 (s, 2H, $C\underline{H}_2$Ar), 7.25-7.39 (m, 5H, Ar-<u>H</u>); MS (EI) *m/e* 182 (M^+, 8), 123 (8), 107 (11), 91 (100), 77 (12), 65 (13), 32 (44); IR (thin film) 3680-3140(m), 3080 (m), 3040 (m), 2940 (s), 2870 (s), 1500 (m), 1370 (m), 1280 (m), 1210 (m), 1110 (s), 1030 (m), 740 (s), 700 (s). This compound was unstable and was further characterised as the disulfide.

3-(Phenylmethyl)oxypropyl disulfide

3-(Phenylmethyl)oxypropan-1-thiol (1g, 5.49mmol) was stirred with potassium hexacyanoferrate (III) (9.0g, 27.5mmol) in aqueous sodium hydroxide solution (1.5M, 20 ml) for 1 hour at room temperature. The mixture

was poured onto ice / water (200ml) and extracted with petroleum ether (3 x 50ml). The combined petrol extracts were dried ($MgSO_4$) and concentrated. Flash chromatography (silica, 60g, eluent 5% ethyl acetate / petroleum ether) gave *3-(phenylmethyl)oxypropyl disulfide* (410mg, 1.13mmol, 42%) as a colourless oil: ^{1}H NMR (300MHz, $CDCl_3$) δ 1.98 (quintet, J 6.9, 4H, C$\underline{H}_2$-2 x 2), 2.78 (t, J 6.9, 4H, C$\underline{H}_2$-1 x 2), 3.55 (t, J 6.9, 4H, C$\underline{H}_2$-3 x 2), 4.49 (s, 4H, C$\underline{H}_2$Ar x 2), 7.23-7.48 (m, 10H, Ar-$\underline{H}$); ^{13}C NMR (75MHz, $CDCl_3$) δ 29.34 (CH_2-2), 35.59 (CH_2-1), 68.38 (CH_2-3), 72.93 (CH_2-Ph), 127.54 (CH-Ar), 128.31 (CH-Ar), 138.40 (C-Ar); MS (EI), *m/e* 362 (M^+, 8), 180 (4), 165 (16), 107 (20), 91 (100), 74 (16), 65 (16); IR (thin film) 3085 (w), 3060 (w), 3030 (m), 2920 (s), 2850 (s), 1495 (w), 1360 (m), 1205 (m), 1100 (s), 1030 (m), 735 (s), 695 (s); Analysis calculated for $C_{28}H_{26}O_2S_2$: C, 66.26; H, 7.23; S, 17.69; Found: C, 66.20, H, 7.25; S, 17.60.

(±)-2-(Phenylmethyl)oxypropylthiomethyl)-(2R,3S*)-3-propyloxirane* (table 1, entry 7).
3-(Phenylmethyl)oxypropan-1-thiol (1.0g; 5.49mmol) was stirred with sodium metal (190mg, 8.24mmol) in diethyl ether (10 ml) for 12 hours then concentrated. *N,N*-dimethyl formamide (10ml) was added to dissolve the white precipitate and the solution decanted from the sodium metal residues. (±)-2-[*p*-Toluenesulfonyloxymethyl]-(2*S**,3*S**)-3-propyloxirane (1.78g, 6.59mmol) was added and the mixture stirred at 60°C for 2 days, then allowed to cool to room temperature. Water (100ml) was added and the mixture washed with petroleum ether (5 x 25 ml). The combined petrol washings were dried ($MgSO_4$), filtered and concentrated. Flash chromatography (silica, 50g, eluent 5% ethyl acetate / 95% petroleum ether, followed by 10% ethyl acetate / 90% petroleum ether then 25% ethyl acetate / petroleum ether) gave *(±)-2-(phenylmethyl)oxypropylthiomethyl)-(2R*,3S*)-3-propyloxirane* (**5f**) (748mg, 2.67mmol, 49% yield) as a yellow oil: ^{1}H NMR (300MHz, $CDCl_3$) δ 0.95 (t, J 6.9, 3H, C$\underline{H}_3$CH$_2$), 1.40-1.65 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 1.90 (quintet, J 6.5, 4H, C$\underline{H}_2$-2 x 2), 2.57 (dd, J 13.9, 5.8, 1H, one of C$\underline{H}_2$-1), 2.68-2.81 (m, 4H, C$\underline{H}$-3 + C$\underline{H}_2$-1' + remaining C$\underline{H}_2$-1), 2.88 (td, J 5.8, 2.0, 1H, C$\underline{H}$-2), 3.57 (t, J 6.5, 2H, C$\underline{H}_2$-3'), 4.51 (s, 2H, C$\underline{H}_2$Ph), 7.26-7.38 (m, 5H, Ar-$\underline{H}$); ^{13}C NMR (75MHz, $CDCl_3$) δ 13.43, 18.70, 28.44 , 29.39, 33.25, 57.24, 57.84, 68.03, 72.27, 126.93, 127.73, 137.95; MS (EI), *m/e* 280 (M^+, 0.4), 262 (M^+-H_2O, 0.5), 237 (1), 180 (17), 91 (100), 74 (26), 65 (12), 57 (16), 55 (17), 43 (16), 41 (16); IR (thin film) 3080 (w), 3040 (w), 2980 (s), 2945 (s), 2880 (s), 1735 (m), 1500 (w), 1460 (m), 1370 (m), 1110 (s), 1035 (m), 920 (m), 745 (s), 705 (s); Analysis calculated for $C_{16}H_{24}O_2S$: C, 68.53; H, 8.63; S, 11.43; Found: C, 68.45, H, 8.40; S, 11.55.

Table 2: Thiiranium ion trapping experiments with silylated nitrogen heterocycles and amide nucleophiles.

Typical procedure:
(±)-1-[(2'R,3'S*)-2'-Phenylthio-3'-hydroxyhexyl]-2-pyridone* (table 2, entry 1)
Trimethylsilyl trifluoromethane sulfonate (0.111ml, 1.15mmol) was added to (±)-2-[(phenylthio)methyl]-(2*R**,3*S**)-3-propyloxirane (**5a**) (100mg, 0.481mmol) in dichloromethane (5ml) at -78°C and stirred for 10 min. *O*-Trimethylsilyl-2-pyridone (96.0mg, 0.577mmol) was added and the reaction mixture allowed to warm to room temperature and stirred for 1 hour. Potassium carbonate (100mg, 0.722mmol) and methanol (5ml) were added and stirring continued for a further 1 hr, then concentrated. Flash chromatography (silica, 10g, eluent 75% ethyl acetate / 1% ethanol / petroleum ether) gave *(±)-1-[(2'R*,3'S*)-2'-phenylthio-3'-hydroxyhexyl]-2-pyridone* (118mg, 0.391mmol, 81%) as a colourless oil: ^{1}H NMR (300MHz, $CDCl_3$) δ 0.90 (t, J 7.1, 3H, C$\underline{H}_3$-6'), 1.41-1.61 (m, 3H, C$\underline{H}_2$-5' + one of C$\underline{H}_2$-4'), 1.82-1.85 (m, 1H, remaining C$\underline{H}_2$-4'), 3.56 (ddd, J 7.9, 5.4, 3.3, 1H, C$\underline{H}$-2'), 3.63 (ddd, J 7.8, 5.3, 3.7, 1H, C$\underline{H}$-3'), 4.11 (dd, J 14.0, 3.3, 1H, 1 of C$\underline{H}_2$-1'), 4.46 (dd, J 14.0, 5.4, remaining C$\underline{H}_2$-1'), 6.21 (t, J 6.6, 1H, C$\underline{H}$-5), 6.57 (d, J 9.0, 1H, C$\underline{H}$-3), 7.22-7.40 (m, 7H, C$\underline{H}$-4 + C$\underline{H}$-6 + Ar$\underline{H}$); ^{13}C NMR (300MHz, $CDCl_3$) δ 13.40 (CH_3-6'), 18.62 (CH_2-5'), 36.06 (CH_2-4'), 49.53 (CH-2'), 54.39 (CH-3'), 70.36 (CH_2-1'), 105.63 (C$\underline{H}$-5), 119.96 (C$\underline{H}$-3), 126.67 (CH-Ar), 128.93 (CH-Ar), 130.31 (CH-Ar), 134.02 (C-Ar), 139.59 (C$\underline{H}$-4), 139.44, 139.86 (CH-6), 163.24 (C-2); IR (thin film) 3600-3100 (s, broad), 3080 (w, Ar C-H), 2960, 2935 (s, C-H), 2870 (m), 1740 (w), 1655 (s, C=O), 1580 (s), 1540 (m), 1480 (m), 1150 (m), 1025 (m), 845 (m), 760 (m), 730 (s), 690 (m); MS *m/e* 304 (M^+)(16), 286 (M^+-H_2O)(10), 260 (8), 231 (18), 208 (40), 194 (11), 190 (15), 176 (79), 166 (84), 136 (100), 123 (18), 109 (51), 96 (60), 78 (38), 67 (35); Accurate mass calculated for $C_{17}H_{21}NO_2S$, 303.129; found 303.130.

Analogous procedures were used to prepare the following:

(±)-1-[(2'R,3'S*)-2'-Methylthio-3'-hydroxyhexyl]-2-pyridone* (table 2, entry 2).

After generation of the thiiranium ion and addition of nucleophile, the reaction was left at rt for 1h prior to work-up. Flash chromatography (silica, 10g, eluent 89% ethyl acetate / 1% ethanol / petroleum ether) gave *(±)-1-[(2'R*,3'S*)-2'-methylthio-3'-hydroxyhexyl]-2-pyridone* (85% yield) as a colourless oil: ^{1}H NMR (300MHz, $CDCl_3$) δ 0.94 (t, J 7.1, 3H, C$\underline{H}_3$-6'), 1.40-1.61 (m, 3H, C$\underline{H}_2$-5' + one of C$\underline{H}_2$-4'), 1.76-1.81 (m, 1H, remaining C$\underline{H}_2$-4'), 2.03 (s, 3H, C$\underline{H}_3$S), 2.96 (ddd, J 7.5, 6.3, 3.6, 1H, C$\underline{H}$-2'), 3.55 (ddd, J 8.6, 7.5, 3.2, 1H, C$\underline{H}$-3'), 4.19 (dd, J 13.8, 3.6, 1H, 1 of C$\underline{H}_2$-1'), 4.32 (dd, J 13.8, 6.3, 1H, remaining C$\underline{H}_2$1'), 6.24 (t, J 6.9, 1H, C$\underline{H}$-5), 6.59 (d, J 9.0, 1H, C$\underline{H}$-3), 7.41 (dd, J 9.0, 6.9, 1H, C$\underline{H}$-4), 7.48 (d, J 6.9, 1H, C$\underline{H}$-6); ^{13}C NMR (300MHz, $CDCl_3$) δ 13.97 (CH_3-6'), 15.10 (SCH_3), 19.11 (CH_2-5'), 36.19 (CH_2-4'), 50.52 (CH-2'), 53.46 (CH-3'), 70.82 (CH_2-1'), 105.87 (CH-5), 120.32 (CH-3), 139.59 (CH-4), 140.11 (CH-6), 163.44 (C-2); IR (thin film) 3700-3000 (s, broad), 2940 (s, C-H), 1660 (s, C=O), 1570 (s), 1540 (m), 1475 (m), 1150 (m), 1020 (m), 850 (m), 770 (s), 740 (m); MS *m/e* 242 (M^+)(3), 223 (M^+-H_2O)(6), 176 (38), 169 (11), 148 (8), 128 (13), 120 (9), 104 (96), 96 (73), 91 (36), 84 (51), 74 (100), 67 (32), 41 (48); Accurate mass calculated for $C_{12}H_{19}NO_2S$, 241.114; found 241.114.

(±)-1-[(2'R,3'S*)-2'-Phenylthio-3'-hydroxyhexyl]uracil* (table 2, entry 3).

After generation of the thiiranium ion and addition of nucleophile, the reaction was left at rt for 1h prior to work-up. Flash chromatography (silica, 10g, eluent 74% ethyl acetate / 1% ethanol / petroleum ether) gave *(±)-1-[(2'R*,3'S*)-2'-phenylthio-3'-hydroxyhexyl]uracil* (75% yield) as colourless plates: m.p. 155-157°C, ^{1}H NMR (300 MHz, $CDCl_3$), δ 0.89 (t, J 7.2, 3H, C$\underline{H}_3$-6'), 1.37-1.68 (m, 4H, C$\underline{H}_2$-4' + C$\underline{H}_2$-5'), 3.60 (dd, J 12.9, 10.5, 1H, 1 of C$\underline{H}_2$-1'), 3.69 (ddd, J 10.5, 4.2, 3.3, 1H, C$\underline{H}$-2'), 3.81 (dt, J 8.3, 4.2, 1H, C$\underline{H}$-3'), 4.33 (dd, J 12.9, 3.3, 1H, remaining C$\underline{H}_2$-1'), 5.44 (d, J 7.8, 1H, C$\underline{H}$-6), 7.10-7.28 (m, 5H, Ar-$\underline{H}$), 7.49 (d, J 7.8, 1H, C$\underline{H}$-5); ^{13}C NMR (75 MHz, CD_3OD) δ 14.20 (CH_3-6'), 20.21 (CH_2-5'), 37.99 (CH_2-4'), 52.19 (CH-2'), 55.59 (CH-3'), 73.84 (CH_2-1'), 101.58 (CH-5), 127.93 (CH-Ar), 130.06 (CH-Ar), 131.87 (CH-Ar), 136.37 (C-Ar), 148.42 (CH-6), 152.78 (C-4), 166.60 (C-2); MS (EI) *m/e* 320 (M^+, 0.2), 302 (M^+-H_2O, 1), 248 (20), 190 (23), 136 (100), 109 (18); IR (nujoll mull) 3390 (m), 3130 (w), 1690 (s), 1650 (s), 1605 (m), 1450 (s), 1405 (m), 1365 (m), 1225 (m), 1180 (m), 1110 (m), 720 (m); Analysis calculated for $C_{16}H_{20}N_2O_3S$: C 59.98, H 6.29, N 8.74, S 10.01, found: C 59.70, H 6.15, N 8.70, S 10.05.

(±)-1-[(2'R,3'S*)-2'-Methylthio-3'-hydroxyhexyl]uracil* (table 2, entry 4).

After generation of the thiiranium ion and addition of nucleophile, the reaction was left at rt for 1h prior to work-up. Flash chromatography (silica, eluent 89% ethyl acetate / 1% ethanol / petroleum ether) gave *(±)-1-[(2'R*,3'S*)-2'-methylthio-3'-hydroxyhexyl]uracil* (81% yield) as colourless plates: m.p. 140-142°C; ^{1}H NMR (300MHz, $CDCl_3$), δ 0.96 (t, J 7.2, 3H, C$\underline{H}_3$-6'), 1.25-1.72 (m, 4H, C$\underline{H}_2$-4' + C$\underline{H}_2$-5'), 2.10 (s, 3H, C$\underline{H}_3$S), 2.92 (ddd, J 7.5, 4.2, 3.9, 1 H, C$\underline{H}$-2'), 3.66-3.78 (m, 2H, C$\underline{H}$-3' + one of C$\underline{H}_2$-1'), 4.20 (dd, J 13.4, 3.9, 1H, remaining C$\underline{H}_2$-1'), 5.70 (d, J 7.9, 1H, C$\underline{H}$-6), 7.31 (d, J 7.9, 1H, C$\underline{H}$-5), 9.60 (s, 1H, N$\underline{H}$); ^{13}C NMR (75 MHz, CD_3OD) δ 14.24 (CH_3-6'), 14.80 (CH_3S), 20.09 (CH_2-5'), 37.85 (CH_2-4'), 50.66 (CH-2'), 53.68 (CH-3'), 73.51 (CH_2-1'), 101.46 (CH-5), 148.41 (CH-6), 152.80 (C-4), 166.60 (C-2); MS (EI) *m/e* 258 (M^+, 0.1), 240 (M^+-H_2O, 2), 186 (14), 128 (30), 113 (45), 104 (17), 82 (17), 74 (100), 55 (18), 41 (33); IR (nujoll mull) 3600-3300 (m), 3160 (w), 1720 (s), 1660 (s), 1470 (s), 1420 (m), 1380 (m), 1285 (m), 1260 (s), 1200 (m), 1180 (m), 1135 (m), 1060 (m), 950 (m), 815 (m), 775 (m), 730 (m), 660 (m); Analysis calculated for $C_{11}H_{18}N_2O_3S$: C, 51.14; H, 7.02; N, 10.84; S, 12.41; Found: C, 51.30; H, 7.10; N, 10.55; S, 12.35.

(+)-1-[(2'R,3'R)-2'-Phenylthio-3'-hydroxyhexyl]uracil (table 2, entry 5).

After generation of the thiiranium ion and addition of nucleophile, the reaction was left at 0°C overnight prior to work-up. Purification by chromatography on 10g silica gel (eluent 74% ethyl acetate / 1% ethanol / 25% petroleum ether) gave *(+)-1-[(2'R,3'R)-2'-phenylthio-3'-hydroxyhexyl]uracil* (55% yield) as colourless plates, mp 141-142°C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 0.92 (t, J 7.1, 3H, C$\underline{H}_3$-6'), 1.35-1.82 (m, 4H, C$\underline{H}_2$-4' + C$\underline{H}_2$-5'), 3.63 (t, J 8.6, $J_{CH2'-CH3'}$ *ca.* 0 Hz, 1H, C$\underline{H}$-2'), 3.74-3.86 (m, 2H, C$\underline{H}$-3' + one of C$\underline{H}_2$-1'), 4.25 (dd, J 13.0, 8.6, 1H, remaining C$\underline{H}_2$-1'), 5.65 (d, J 10.0, 1H, C$\underline{H}$-5), 7.22-7.38 (m, 6H, Ar-$\underline{H}$ + C$\underline{H}$-6), 8.65 (brs, 1H, N$\underline{H}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.90 (CH_3-6'), 19.07 (CH_2-5'), 37.29 (CH_2-4'), 52.33 (CH-2), 54.23 (CH-3), 70.88 CH_2-1'), 101.73 (CH-5), 127.32 (CH-Ar), 129.29 (CH-Ar), 131.02 (CH-Ar), 134.04

(C-Ar), 145.63 (CH-6), 150.90 (C-4), 163.25 (C-2); MS (EI) *m/e* 320 (M^+, 1), 302 (M^+-H_2O, 2), 248 (19), 190 (29), 136 (100), 109 (9); IR (nujoll mull) 3640-3100 (m), 2945 (s), 2920 (s), 2860 (m), 1690 (m), 1660 (s), 1455 (s), 1375 (m), 1240 (m), 1190 (m), 1130 (m), 1120 (m), 1075 (m), 1045 (m), 1020 (m), 950 (m), 855 (m), 825 (m), 735 (m), 685 (m); Analysis: calculated for $C_{16}H_{20}N_2O_3S$ C 59.98, H 6.29, N 8.74, S 10.01, found C 60.01, H 6.33, N 8.82, S 10.10; $[\alpha]_D^{20}$ +36.6° (*c* 1.18, ethanol).

(±)-1-[(2'R,3'R*)-2'-Methylthio-3'-hydroxyhexyl]uracil* (table 2, entry 6).
After generation of the thiiranium ion and addition of nucleophile, the reaction was left at 0°C overnight prior to work-up. Purification by chromatography on 5g silica gel (eluent 74% ethyl acetate / 1% ethanol / 25% petroleum ether) gave *(±)-1-[(2'R*,3'R*)-2'-methylthio-3'-hydroxyhexyl]uracil* (68% yield) as colourless plates: mp. 135-137°C; ^{1}H NMR (300MHz, $CDCl_3$), δ 0.95 (t, J 6.9, 3H, C<u>H</u>$_3$-6'), 1.22-1.78 (m, 4H, C<u>H</u>$_2$-4' + C<u>H</u>$_2$-5'), 2.14 (s, 3H, C<u>H</u>$_3$S), 2.96 (ddd, J 7.5, 6.5, 2.5, 1 H, C<u>H</u>-2'), 3.65-3.75 (brm, 1H, C<u>H</u>-3'), 3.77 (dd, J 14.0, 7.5, 1H, one of C<u>H</u>-1'), 4.17 (dd, J 14.0, 6.5, 1H, remaining C<u>H</u>$_2$-1'), 5.72 (d, J 7.8, 1H, C<u>H</u>-6), 7.35 (d, J 7.8, 1H, C<u>H</u>-5), 9.80 (s, 1H, N<u>H</u>); MS (CI, NH_3) 276 (M^++18), 259(M^++1); IR (thin film) 3435 (w, br, NH stretch), 2957 (m), 2872 (m, C-H stretch), 1685 (s, C=O stretch), 1460 (m), 1238 (m); Accurate mass calculated for M^++1: 259.112, found: 259.112.

(±)-1-[(2'R,3'S*)-2'-(Phenylmethyl)thio-3'-hydroxyhexyl]uracil* (table 2, entry 7).
After generation of the thiiranium ion and addition of nucleophile, the reaction was left at 0°C overnight prior to work-up. Flash chromatography (silica, 10g, eluent 74% ethyl acetate / 1% ethanol / petroleum ether) gave *(±)-1-[(2'R*,3'S*)-2'-(phenylmethyl)thio-3'-hydroxyhexyl]uracil* (80mg, 0.240mmol, 53% yield) as colourless needles: m.p. 132-133°C; ^{1}H NMR δ 0.92 (t, J 6.7, 3H, C<u>H</u>$_3$-6'), 1.37-1.53 (m, 3H, C<u>H</u>$_2$-5' + one of C<u>H</u>$_2$-4'), 1.60-1.65 (m, 1H, remaining C<u>H</u>$_2$-4'), 2.88 (brm, 1H, C<u>H</u>-2'), 3.51 (dd, J 14.6, 10.0, 1H, 1 of C<u>H</u>$_2$-1'), 3.60-3.78 (m, 3H, including AB system δ 3.66, Δν 18.0, J 12.2, 2H, C<u>H</u>$_2$Ph + 1H, C<u>H</u>-3'), 4.05 (dd, J 14.6, 5.0, 1H, remaining C<u>H</u>$_2$-1'), 5.62 (d, J 9.8, 1H, C<u>H</u>-5), 7.10-7.38 (m, 6H, Ar-<u>H</u> +C<u>H</u>-6), 9.10 (brs, 1H, N<u>H</u>); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.95 (CH_3-6'), 19.12 (CH_2-5'), 35.85 (CH_2-4'), 36.89 (CH_2Ph), 49.54 (CH-2'), 50.53 (CH-3'), 72.25 (CH_2-1'), 101.12, 128.78, 137.45, 146.16, 150.94, 163.69; MS (EI) *m/e* 334 (M^+, 0.1), 316 (M^+-H_2O, 1), 262 (11), 195 (11), 150 (39), 113 (13), 91 (100); IR (nujoll mull) 3400 (m), 1740 (s), 1700 (s), 850 (m), 770 (m), 740 (m); Analysis: calculated for $C_{17}H_{22}N_2O_3S$, C 61.05, H 6.63, N 8.38, S 9.59, found C 61.15, H 6.65, N 8.25, S 9.50.

(±)-1-[(2'R,3'S*)-2'-(Phenylmethyl)oxypropylthiomethyl-3'-hydroxyhexyl]uracil* (table 2, entry 8).
After generation of the thiiranium ion and addition of nucleophile, the reaction was left at room temperature for 2h prior to work-up. Chromatography on silica gel (flash grade, 5g, eluent 3:1 ethyl acetate : petrol) gave the uracil (20% yield) as colourless plates: ^{1}H NMR ($CDCl_3$, 300MHz) δ 0.95 (t, J 6.8, 3H, CH_3-6'), 1.25-1.68 (m, 4H, CH_2-5'; CH_2-4'), 1.83 (quintet, J 6.1, 2H, CH_2-2"), 2.63 (t, J 6.1, 2H CH_2-3" (next to S)), 2.99 (ddd, J 7.6, 4.7, 3.8 1H, CH_2-2'), 3.51 (t, J 6.1, 2H, CH_2-1"), 3.64-3.72 (m, 2H, CH_2-3' + one of CH_2-1'), 4.15 (dd, J 14.6, 3.8, 1H remaining CH_2-1'), 4.48 (s, 2H, CH_2Ph), 5.65 (d, J 7.9, 1H, CH-5), 7.24-7.36 (m, 6H, CH-6 + C_6H_5), 8.23 (brs, 1H, uracil NH); MS (CI, NH_3) *m/e* 410 (M+18, 52), 392 (M+1, 55), 228 (100), 211 (100), 198 (64), 181 (38), 108 (33), 91 (30); IR (thin film) 2923 (m), 2853 (m), 1683 (s), 1463 (m), 1365 (w), 1261 (w), 1100 (w), 1029 (w), 809 (w), 739 (w), 699 (w).

(±)-1-[(2'R,3'S*)-2'-Phenylthio-3'-hydroxyhexyl]imidazole* (table 2, entry 9).
After generation of the thiiranium ion and addition of nucleophile, the reaction was left at 0°C for 48h prior to work-up. Flash chromatography (silica, 5g, eluent 74% ethyl acetate / 1% ethanol / petroleum ether) gave *(±)-1-[(2'R*,3'S*)-2'-phenylthio-3'-hydroxyhexyl]imidazole* (39% yield) as a yellow oil: ^{1}H NMR δ 0.92 (t, J 7.0, 3H, C<u>H</u>$_3$-6'), 1.23-1.70 (m, 4H, C<u>H</u>$_2$-4' + C<u>H</u>$_2$-5'), 3.13 (dt, J 7.2, 4.8, 1H, C<u>H</u>-2'), 3.67 (ddd, J 8.6, 4.8, 4.2, 1H, C<u>H</u>-3'), 4.21 (dd, J 14.4, 7.2, 1H, one of C<u>H</u>$_2$-1'), 4.29 (dd, J 14.4, 4.8, 1H, remaining C<u>H</u>$_2$-1'), 7.00 (d, J 15.0, 2H, C<u>H</u>-4 + C<u>H</u>-5), 7.22-7.38 (m, 5H, Ar-<u>H</u>), 7.56 (s, 1H, C<u>H</u>-2); MS (EI) *m/e* 276 (M^+, 15), 167 (M^+-SPh, 13), 136 (100), 123 (16),109 (42), 91 (19), 82 (17), 81 (23), 77 (16), 69 (47), 65 (17), 57 (25), 55 (34); IR (thin film) 3600-3000 (s, OH),3080 (m), 2960 (s), 2940 (m), 2880 (m), 1580 (s), 1520 (m), 1480 (s), 1440 (s), 1390 (m), 1330 (m), 1150 (m), 1130 (m), 1080 (s), 1025 (s), 970 (m), 920 (m), 740 (s), 690 (s), 660 (m); Analysis: calculated for $C_{15}H_{20}N_2OS$: C, 65.18; H, 7.29; N, 10.14; S, 11.60; found:

C,65.45; H, 7.10; N, 9.75; S, 11.60); Epoxy sulfide (±)-(**5a**) (44%) was also recovered.

(±)-1-[(2'R,3'S*)-2'-Methylthio-3'-hydroxyhexyl]imidazole* (table 2, entry 10).
After generation of the thiiranium ion and addition of nucleophile, the reaction was left at 0°C for 48h prior to work-up. Flash chromatography (magnesium silicate, 5g, eluent 89% ethyl acetate /1% ethanol/ petroleum ether) gave *(±)-1-[(2'R*,3'S*)-2'-methylthio-3'-hydroxyhexyl]imidazole* (33% yield) as a yellow oil: ^{1}H NMR δ 0.95 (t, J 9.0, 3H, C$\underline{H}_3$-6'), 1.26-1.65 (m, 4H, C$\underline{H}_2$-4' + C$\underline{H}_2$-5'), 1.93 (s, 3H, SC$\underline{H}_3$), 2.77 (dt, J 8.2, 4.1, 1H, C$\underline{H}$-2'), 3.66 (dt, J 8.6, 4.1, 1H, C$\underline{H}$-3'), 4.14 (dd, J 14.4, 8.1, 1H, one of C$\underline{H}_2$-1'), 4.32 (dd, J = 14.4, 4.2, 1H, remaining C$\underline{H}_2$-1'), 7.05 (d, J 15.0, 2H, C$\underline{H}$-4 + C$\underline{H}$-5), 7.58 (brs, 1H, C$\underline{H}$-2); MS (EI) *m/e* 214 (M^+, 6), 167 (M^+-SMe, 50), 99 (13), 85 (14), 82 (28), 81 (24), 74 (71), 69 (100), 61 (16), 57 (29), 55 (28), 43 (23), 41 (39); IR (thin film) 3700-3120 (s, OH), 2960 (s), 2920 (s), 2870 (m), 1500 (m), 1535 (s), 1285 (m), 1225 (s), 1155 (m), 1120 (m), 1075 (s), 1025 (m), 960 (m), 915 (m), 815 (m), 735 (s), 655 (s).

(±)-N-[(2'R,3'S*)-2'-Phenylthio-3'-hydroxyhexyl]acetamide* (table 2, entry 11).
After generation of the thiiranium ion and addition of nucleophile, the reaction was left at 0°C for 6h prior to work-up. Flash chromatography (silica, 5g, eluent 74% ethyl acetate / 1% ethanol / petroleum ether) gave *(±)-N-[(2'R*,3'S*)-2'-phenylthio-3'-hydroxyhexyl]acetamide* (58% yield) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, J 7.6, 3H, C$\underline{H}_3$CH$_2$), 1.37-1.59 (m, 3H, 3 of CH$_2$C$\underline{H}_2$), 1.79-1.87 (m, 1H, remaining C$\underline{H}_2$C$\underline{H}_2$), 2.02 (s, 3H, C$\underline{H}_3$CO), 3.17 (ddd, J 7.4, 6.7, 4.3, 1H, C$\underline{H}$-2'), 3.32 (dt, J 15.0, 4.3, 1H, one of C$\underline{H}_2$-1'), 3.52 (dt, J 7.4, 2.5, 1H, C$\underline{H}$-3'), 3.88 (ddd, J 15.0, 6.7, 3.5, 1H, remaining C$\underline{H}_2$-1'), 4.32 (brs, 1H,O$\underline{H}$), 6.15 (brm, 1H, N$\underline{H}$), 7.25-7.32 (m, 5H, Ar-$\underline{H}$); ^{13}C NMR δ 13.9 (CH_3-6'), 19.0 (CH_2-5'), 23.0 (CH_3-2), 36.3 (CH_2-4'), 39.6 (CH-3'), 55.6 (CH-2'), 70.5 (CH_2-1'), 127.3 (CH-Ar), 129.2 (CH-Ar), 131.6 CH-(Ar), 134.3 (C-Ar), 171.6 (C-1), MS *m/e* 267 (0.2) (M^+), 249 (5) (M^+-H_2O), 195 (25), 190 (24), 136 (100), 109 (22), 43 (58); IR (thin film) 3700-3150 (s, broad), 3100 (w), 2980 (s), 2960 (s), 2880 (m), 1640 (s, C=O), 1550 (s), 1450 (m), 1380 (m), 1300 (m), 1020 (m), 860 (m), 750 (s), 700 (s); Analysis calculated for $C_{14}H_{21}NO_2S$: C, 62.89; H, 7.92; N, 5.24; S, 11.99; found: C, 62.85; H, 8.15; N, 5.00; S, 12.10.

(±)-N-[(2'R,3'S*)-2'-Methylthio-3'-hydroxyhexyl]acetamide* (table 2, entry 12).
After generation of the thiiranium ion and addition of nucleophile, the reaction was left at 0°C for 56h prior to work-up. Column chromatography on magnesium silicate (TLC grade florisil, 5g, eluent 10% ethyl acetate / petroleum ether) gave *(±)-N-[(2'R*,3'S*)-2'-methylthio-3'-hydroxyhexyl]acetamide* (64% yield) as a colourless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, J 7.2, 3H, C$\underline{H}_3$-6'), 1.25-1.64 (m, 3H, C$\underline{H}_2$-5' + one of C$\underline{H}_2$-4'), 1.72-1.83 (m, 1H, remaining C$\underline{H}_2$-4'), 2.02 (s, 3H, C$\underline{H}_3$-2), 2.15 (s, 3H, C$\underline{H}_3$S), 2.56 (ddd, J 8.1, 7.5, 3.4, 1H, C$\underline{H}$-2'), 3.37 (ddd, J 15.0, 5.8, 3.4, 1H, one of C$\underline{H}_2$-1'), 3.44 (td, J 8.1, 2.6, 1H, C$\underline{H}$-3'), 3.87 (ddd, J 15.0, 7.5, 4.3, 1H, remaining C$\underline{H}_2$-1'), 4.00 (brs, 1H, O$\underline{H}$), 6.15 (brm, 1H, N$\underline{H}$); MS *m/e* 205 (M^+, 0.04),187 (M^+-H_2O, 4), 195 (25), 133 (23), 128 (33), 90 (20), 74 (100), 60 (17), 43 (53), 41 (18); IR (thin film) 3710-3140 (s, broad), 2985 (s), 2965 (s), 2880 (m), 1645 (s, C=O), 1555 (s), 1440 (m) 1375 (m), 1295 (m), 1125 (m), 1080 (w) 1015 (m), 855 (m), 745 (m); Analysis calculated for $C_9H_{19}NO_2S$: C, 52.65, H 9.33, N 6.82, S 15.62; found: C, 52.80, H 9.45, N, 6.75, S 15.40.

(+)-N-[(2'R,3'R)-2'-Phenylthio-3'-hydroxyhexyl]acetamide (table 2, entry 13).
After generation of the thiiranium ion and addition of nucleophile, the reaction was left at 0°C for 3 days prior to work-up. Flash chromatography(silica, 5g, eluent 49% ethyl acetate / 1% ethanol / petroleum ether, followed by 74% ethyl acetate / 1% ethanol / 25% petroleum ether) gave *(+)-N-[(2'R,3'R)-2'-phenylthio-3'-hydroxyhexyl]acetamide* (40% yield) as a colourless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, J 8.6, 3H, C$\underline{H}_3$-6'), 1.23-1.78 (m, 4H, C$\underline{H}_2$-4' + C$\underline{H}_2$-5'), 1.95 (s, 3H, C$\underline{H}_3$-2), 3.21 (t, J 7.6, $J_{CH2'-CH3'}$ = 0 approx, 1H, C$\underline{H}$-2'), 3.29 (dd, J 14.6, 4.6, 1H, one of C$\underline{H}_2$-1'), 3.52 (brs, 1H, O$\underline{H}$), 3.75-3.85 (m, 2H, C$\underline{H}$-3' + remaining C$\underline{H}_2$-1'), 6.43 (brm, 1H, N$\underline{H}$), 7.20-7.33 (m, 3H, *m*- + *p*-Ar-$\underline{H}$), 7.43 (d, 2H, *o*-Ar-$\underline{H}$); ^{13}C NMR δ 13.97 (CH_3-6'), 19.18 (CH_2-5'), 23.14 ($\underline{C}H_3$-2), 36.73 (CH_2-4'), 41.79 (CH_2-1'), 55.78 (CH-2), 70.91 (CH-3), 127.21 (CH-Ar), 129.16 (CH-Ar), 131.81 (CH-Ar), 134.67 (C-Ar), 171.06 (C-1), MS *m/e* 267 (M^+, 0.5), 249 (M^+-H_2O, 5), 195 (19), 190 (32), 140 (33), 136 (100), 109 (11); IR (nujoll mull) 3270 (s), 1625 (s, C=O), 1555 (m), 1450 (s), 1370 (s), 1305 (m), 1285 (m), 1120 (m), 1080 (m), 955 (s), 720 (s), 685 (m); Analysis calculated for $C_{14}H_{21}NO_2S$: C, 62.89, H 7.92, N 5.24, S 11.99; found: C, 62.60, H 7.85, N, 5.25, S 12.05;

$[\alpha]_D^{20}$ +47.6° (*c* 0.97, ethanol).

(±)-N-[(2'R,3'R)-2'-Methylthio-3'-hydroxyhexyl]acetamide (table 2, entry 14).
After generation of the thiiranium ion and addition of nucleophile, the reaction was left at 0°C for 3 days prior to work-up. Flash chromatography (magnesium silicate, 5g, eluent 40% ethyl acetate / 1% ethanol / petroleum ether followed by 74% ethyl acetate / 1% ethanol / petroleum ether) gave *(±)-N-[(2'R,3'R)-2'-methylthio-3'-hydroxyhexyl]acetamide* (44% yield) as a colourless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, J 7.1, 3H, C$\underline{H}_3$-6'), 1.30-1.74 (m, 4H, C$\underline{H}_2$-4' + C$\underline{H}_2$-5'), 2.04 (s, 3H, SC$\underline{H}_3$), 2.12 (s, 3H, C$\underline{H}_3$-2), 2.65 (ddd, J 10.5, 7.5, 4.0, C$\underline{H}$-2'), 3.08 (brs, CHO$\underline{H}$), 3.27 (ddd, J 14.3, 7.5, 4.1, C$\underline{H}$-1'), 3.65-3.75 (brm, 1H, C$\underline{H}$-3'), 3.78 (dd, J 14.3, 6.7, C$\underline{H}$-1'), 6.30 (brm, N$\underline{H}$); MS (CI) 206 (M^++1, 100); IR (thin film) 3467 (w, br, N-H stretch), 2958 (s, C-H stretch), 2930 (s, C-H stretch), 1708 (s C=O stretch), 1583 (s), 1480 (s), 1438 (s) 1025 (s), 740 (s) , 691 (s); Analysis calculated for $C_9H_{19}NO_2S$: C, 52.65, H 9.33, N 6.82, S 15.62; found: C, 52.60, H 9.35, N, 6.87, S 15.60.

(±)-N-[(2'R,3'S*)-2'-Phenylmethylthio-3'-hydroxyhexyl]acetamide* (table 2, entry 15).
After generation of the thiiranium ion and addition of nucleophile, the reaction was left at 0°C for 2 days prior to work-up. Chromatography on kieselgel (eluent 25% ethyl acetate / petroleum ether followed by 100 ml 50% ethyl acetate / petroleum ether) gave *(±)-N-[(2'R*,3'S*)-2'-phenylmethylthio-3'-hydroxyhexyl]acetamide* (51% yield) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, J 6.9, 3H, C$\underline{H}_3$-6'), 1.25-1.52 (m, 3H, C$\underline{H}_2$-5' + one of C$\underline{H}_2$-4'), 1.66-1.71 (m, 1H, remaining C$\underline{H}_2$-4'), 1.95 (s, 3H, C$\underline{H}_3$-2), 2.56 (dt, J 7.8, 3.9, 1H, C$\underline{H}$-2'), 3.16 (ddd, J 14.3, 5.6, 3.9, 1H, one of C$\underline{H}_2$-1'), 3.40 (td, J 7.8, 2.9, 1H, C$\underline{H}$-3'), 3.69-3.81 (m, 3H, remaining C$\underline{H}_2$-1' + C$\underline{H}_2$Ph), 4.05 (brs, 1H, O$\underline{H}$), 6.01 (brs, 1H, N$\underline{H}$), 7.23-7.38 (m, 5H, Ar-$\underline{H}$); MS (EI) *m/e* 281 (M^+, 0.1), 263 (M^+-H_2O, 0.7), 172 (14), 149 (19), 118 (13), 91 (100), 65 (12), 60 (12), 55 (10), 43 (29), 41 (13); IR (thin film) 3700-3160 (s, broad), 3000 (s), 2980 (s), 2920 (s), 2880 (m), 1670 (s, C=O), 1580 (m), 1520 (m), 1480 (m), 1400 (m), 1310 (m), 1150 (m), 1095 (m), 1070 (w), 1050 (m), 1030 (m), 790 (m), 725 (s); Accurate mass calculated for M^++1 $C_{15}H_{24}NO_2S$: 282.153, found (CI, NH_3): 282.152.

(±)-N-Methyl-N-[(2'R,3'S*)-2'-phenylthio-3'-hydroxyhexyl]acetamide* (table 2, entry 16).
After generation of the thiiranium ion and addition of nucleophile, the reaction was left at 0°C for 3 days prior to work-up. Flash chromatography (silica, 10g, eluent 49% ethyl acetate / 1% ethanol / petroleum ether) gave *(±)-N-methyl-N-[(2'R*,3'S*)-2'-phenylthio-3'-hydroxyhexyl]acetamide* (55% yield) as a yellow oil: ^{1}H NMR δ 0.90 (t, J 7.1, 3H, C$\underline{H}_3$-6'), 1.39-1.57 (m, 3H, C$\underline{H}_2$-5' + one of C$\underline{H}_2$-4'), 1.70-1.90 (m, 1H, remaining C$\underline{H}_2$-4'), 2.07 (s, 3H, C$\underline{H}_3$-2), 3.08 (s, 3H, NC$\underline{H}_3$), 3.47 (ddd, J 10.1, 6.4, 5.1, 1H, C$\underline{H}$-2'), 3.54-3.60 (m, 2H, C$\underline{H}$-3' + one of C$\underline{H}_2$-1'), 3.86 (dd, J 14.4, 5.1, remaining C$\underline{H}_2$-1'), 7.20-7.45 (m, 5H, Ar-$\underline{H}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0 (CH_3-6'), 19.15 (CH_2-5'), 21.9 (CH_3-2), 36.4 (CH_2-4'), 39.3 (CH_3N), 49.0 (CH-2'), 54.7 (C-3'), 70.9 (C-1'), 126.9 (CH-Ar), 129.2 (CH-Ar), 130.8 (C-Ar), 138.8 (C-1); IR (thin film) 3700-3100 (s, br., NH), 2980 (s), 2940 (s), 2900 (s), 1640 (s), 1420 (m), 1130 (m), 1030 (m), 980 (m), 740 (m); MS (EI), *m/e* 282 (M^++1) (2), 264 (M^++1-H_2O) (7), 209 (19), 190 (7), 178 (9), 166 (29), 154 (100), 136 (64), 123 (12), 109 (24), 100 (17), 86 (35), 77 (14), 65 (14), 57 (25), 44 (94); Accurate mass calculated for M^++1 $C_{15}H_{24}NO_2S$: 282.153, found (CI, NH_3): 282.152.

(±)-N-Methyl-N-[(2'R,3'S*)-2'-methylthio-3'-hydroxyhexyl]acetamide* (table 2, entry 17).
After generation of the thiiranium ion and addition of nucleophile, the reaction was left at 0°C for 3 days prior to work-up. Column chromatography on magnesium silicate (TLC grade florisil, 10g, eluent 49% ethyl acetate / 1% ethanol / petroleum ether) gave *(±)-N-methyl-N-[(2'R*,3'S*)-2'-methylthio-3'-hydroxyhexyl]acetamide* (44% yield) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, J 7.2, 3H, C$\underline{H}_3$-6'), 1.41-1.59 (m, 3H, C$\underline{H}_2$-5' + one of C$\underline{H}_2$-4'), 1.65-1.82 (m, 1H, remaining C$\underline{H}_2$-4'), 2.12 (s, 3H, C$\underline{H}_3$-2), 2.15 (s, 3H, C$\underline{H}_3$S), 2.75 (ddd, J 7.6, 5.6, 3.8, 1H, C$\underline{H}$-2'), 3.16 (s, 1H, NC$\underline{H}_3$), 3.46-3.57 (m, 1H, C$\underline{H}$-3'), 3.57 (dd, J 14.5, 3.8, 1H, one of C$\underline{H}_2$-1'), 3.82 (dd, J 14.5, 5.6, 1H, remaining C$\underline{H}_2$-1'), 4.20 (d, J 4.8, 1H, O$\underline{H}$); ^{13}C NMR δ 13.89 (CH_3-6'), 14.88 (CH_3S), 19.08 (CH_2-5'), 21.75 (CH_3-2), 36.05 (CH_2-4'), 38.75 (CH_3N), 48.50 (CH-2), 53.12 (CH-3), 70.80 (CH_2-1), 171.92 C-1); MS *m/e* M^+not observed, 201 (M^+-H_2O, 1), 154 (50), 147 (14), 104 (14), 86 (28), 74 (57), 55 (13), 44 (100), 41 (18); IR (thin film) 3700-3200 (s, O-H stretch), 2960 (s, C-H stretch), 2940 (m, C-H stretch), 2880 (m, C-H stretch), 1625 (s, C=O), 1475 (m), 1450 (m) 1405 (m), 1355

(m), 1300 (m), 1120 (m), 1020 (m), 735 (m), 685 (m); Analysis calculated for $C_{10}H_{120}NO_2S$: C, 54.76, H 9.65, N 6.39, S 14.62; found: C, 54.85, H 9.40, N, 6.60, S 14.90.

Reduction of acetamide derivative to prove N-alkylation (scheme 2):
(±)-N-[(2'R,3'S*)-2'-Phenylthio-3'-hydroxyhexyl]ethylamine*
(±)-N-[(2'R,3'S*)-2'-Phenylthio-3'-hydroxyhexyl]acetamide* (table 2, entry 11) (45mg, 0.168mmol) was heated under reflux with lithium aluminum hydride (13mg, 0.337mmol) in diethyl ether for 5h and allowed to cool to room temperature. Water (5ml) was added dropwise followed by diethyl ether (5ml) and the layers separated. The aqueous layer was washed with diethyl ether (3x5ml) and the combined ethereal portions dried ($MgSO_4$), filtered and concentrated. Column chromatography on magnesium silicate (TLC grade florisil, 5g, eluent 49% ethyl acetate /1% ethanol / petroleum ether) gave *(±)-N-[(2'R*,3'S*)-2'-phenylthio-3'-hydroxyhexyl]ethylamine* (27mg, 0.108mmol, 64% yield) as a colourless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, J 7.2, 3H, C<u>H</u>$_3$-6'), 1.08 (t, J 7.2, C<u>H</u>$_3$-2), 1.30-1.78 (m, 4H, C<u>H</u>$_2$-4' + C<u>H</u>$_2$-5'), 2.63 (q, J 7.2, 2H, C<u>H</u>$_2$-1), 2.91 (dd, J 13.5, 6.7, 1H, C<u>H</u>$_2$-1'), 3.12 (dd, J 13.5, 4.4, 1H, one of C<u>H</u>$_2$-1'), 3.14 (dt, J 6.8, 4.4, 1H, C<u>H</u>-2'), 3.83 (ddd, J 7.1, 5.2, 4.4, 1H, C<u>H</u>-3'), 7.23-7.37 (m, 4H, *o-* + *m*-Ar-<u>H</u>); 7.43 (d, J 6.7, *p*-Ar-<u>H</u>); MS (CI) 254 (M^++1, 100); IR (thin film) 3295(brs, N-H stretch), 3059 (m, aryl C-H stretch), 2959, 2871 (s, alkyl C-H stretch), 1583 (m), 1480 (s), 1438 (s), 1122 (m), 745 (s, aryl o.o.p.), 692 (s, aryl o.o.p.), accurate mass (CI): calculated for M^++1 $C_{14}H_{24}NOS$ 254.158, found 254.157.

Table 3: Results of thiiranium ion trapping experiments with N-trimethylsilyl amines.

Typical procedures:
(±)-1-[(2'R,3'S*)-2'-Phenylthio-3'-hydroxyhexyl]piperidine* using TMSOTf (table 3, entry 1, method A).
Trimethylsilyl trifluoromethane sulfonate (56mg, 0.289mmol) was added to (±)-2-[(phenylthio)methyl]-(2*R**,3*S**)-3-propyloxirane (**5a**) (50mg, 0.240mmol) in dichloromethane (2ml) at -78°C and stirred for 10min.. 1-Trimethylsilylpiperidine (76mg, 0.481mmol) was added, stirred for 10 min, allowed to warm to 0°C and stirred for a further 72 hours at this temperature. Potassium carbonate (100mg, 0.723mmol) and methanol (2ml) were added and stirring continued for 12 hours at 0°C, and the mixture then concentrated. Dichloromethane (10ml) was added, the mixture shaken and then washed with water (2x2ml). The aqueous washings were back-extracted with dichloromethane (3x5ml) and the combined organic portions dried ($MgSO_4$), filtered and concentrated. Flash chromatography (magnesium silicate, 5g, eluent 5% ethyl acetate / petroleum ether, followed by 10% ethyl acetate / petroleum ether) gave *(±)-1-[(2'R*,3'S*)-2'-phenylthio-3'-hydroxyhexyl]piperidine* (16mg, 0.055mmol, 23% yield) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (t, J 7.0, 3H, C<u>H</u>$_3$-6'), 1.20-1.70 (m, 9H, C<u>H</u>$_2$-3 + C<u>H</u>$_2$-4 + C<u>H</u>$_2$-5 + C<u>H</u>$_2$-5' + one of C<u>H</u>$_2$-4'), 1.90-2.03 (m, 1H, remaining C<u>H</u>$_2$-4'), 2.17-2.43 (m, 2H, two of C<u>H</u>$_2$-2 or C<u>H</u>$_2$-6), 2.43-2.67 (m, 2H, remaining C<u>H</u>$_2$-2 or C<u>H</u>$_2$-6), 2.73 (AB system, Δν 6.8, J 10.4, 2H, C<u>H</u>$_2$-1'), 3.16 (dt, J 10.4, 4.6, 1H, C<u>H</u>-2'), 3.73 (dt, J 11.5, 4.6, 1H, C<u>H</u>-3'), 7.21-7.34 (m, 3H,*o*- and *p*-Ar-<u>H</u>), 7.39 (d, J 7.5, 2H, *m*-Ar-<u>H</u>); MS (EI) *m/e* 293 (M^+, 2), 250 (23), 220 (16), 208 (22), 184 (24), 178 (21), 170 (47), 165 (43), 149 (17), 147 (24), 136 (100), 123 (85), 112 (25), 110 (85); IR (thin film) 3660-3040 (m), 3080 (m), 3060 (m), 2960 (m), 2940 (s), 2860 (m), 2820 (m), 1580 (m), 1480 (s), 1460 (m), 1440 (s), 1380 (m), 1350 (m), 1310 (m), 1270 (m), 1190 (m), 1155 (m), 1135 (s), 1110 (s), 1090 (m), 1070 (m), 1040 (m), 1030 (m), 990 (m), 965 (m), 860 (m), 740 (s), 690 (s); accurate mass calculated for $C_{17}H_{27}NOS$: 293.181, found (EI): 293.182.

(±)-1-[(2'R,3'S*)-2'-Phenylthio-3'-hydroxyhexyl]piperidine* using BF_3•OEt_2 (table 3, entry 2, method B).
Boron trifluoride etherate (68mg, 0.482mmol) was added to a solution of (±)-2-[(phenylthio)methyl]-(2*R**,3*S**)-3-propyloxirane (**5a**) (100mg, 0.482mmol) in dichloromethane (2ml) at -78°C. After stirring for 10 minutes, 1-trimethylsilylpiperidine (76mg, 0.482mmol) was added and stirring continued for a further 10 minutes at this temperature and overnight at 0°C. Potassium carbonate (227 mg, 1.64mmol) and methanol (3ml) was added and stirring continued for 2 hours at room temperature. The reaction mixture was concentrated, then redissolved in dichloromethane (10ml) and washed with water (2 x 2ml). The aqueous washings were back-extracted with dichloromethane (4 x 5 ml) and the combined dichloromethane portions dried ($MgSO_4$), filtered and concentrated. Flash chromatography (kieselgel, 15g, eluent ammonia (0.880 s.g., aq.) / ethanol / dichloromethane, 1:8:1191) gave *(±)-1-[(2'R*,3'S*)-2'-phenylthio-3'-hydroxyhexyl]piperidine* (56mg, 0.191mmol, 40% yield) as a yellow

oil. Spectroscopic data was consistent with previous samples.

(±)-1-[(2'R,3'S*)-2'-Methylthio-3'-hydroxyhexyl]piperidine* (table 3, entry 3).
Prepared from (±)-2-[(methylthio)methyl]-(2*R**,3*S**)-3-propyloxirane (**5b**) (50mg, 0.342mmol) using method A. Flash chromatography (magnesium silicate, 5g, eluent 5% ethyl acetate / petroleum ether, followed by 25% ethyl acetate / 1% ethanol / petroleum ether) gave *(±)-1-[(2'R*,3'S*)-2'-methylthio-3'-hydroxyhexyl]piperidine* (29mg, 0.112mmol, 37% yield) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (t, J 7.0, 3H, C$\underline{H}_3$-6'), 1.37-1.64 (m, 7H, C$\underline{H}_2$-5' + C$\underline{H}_2$-3 + C$\underline{H}_2$-4 + C$\underline{H}_2$-5 + one of C$\underline{H}_2$-4'), 1.86-1.95 (m, 1H, remaining C$\underline{H}_2$-4'), 2.09 (s, 3H SC$\underline{H}_3$), 2.29-2.43 (m, br, 2H, two of C$\underline{H}_2$-2 or C$\underline{H}_2$-6), 2.55 (ddd, J 12.0, 10.5, 4.5, 1H, C$\underline{H}$-2'), 2.57-2.68 (m, br, 2H, remaining C$\underline{H}_2$-2 or C$\underline{H}_2$-6), 2.69 (dd, J 12.8, 10.5, 1H, one of C$\underline{H}_2$-1'), 2.78 (dd, J 12.8, 4.5, 1H, remaining C$\underline{H}_2$-1'), 3.66 (dt, J 10.0, 2.7, 1H C$\underline{H}$-3'); MS (EI) *m/e* 231 (M^+, 5), 194 (13), 188 (100), 184 (55), 170 (18), 166 (11), 159 (45), 150 (11), 146 (27), 142 (17), 140 (35), 137 (11), 124 (12), 121 (23), 116 (17), 110 (54); IR (thin film) 3620 -3040(m), 2960 (s), 2940 (s), 2880 (m), 1470 (m), 1450 (m), 1440 (s), 1375 (m), 1350 (m), 1310 (m), 1275 (m), 1195 (m), 1155 (m), 1135 (s), 1110 (s), 1095 (m), 1070 (m), 1040 (m), 985 (m), 960 (m), 860 (s), 830 (m), 770 (m); accurate mass calculated for $C_{12}H_{25}NOS$: 231.166, found (EI): 231.167.

(±)-1-[(2'R,3'S*)-2'-methylthio-3'-hydroxyhexyl]piperidine* (table 3, entry 4).
Prepared from (±)-2-[(methylthio)methyl]-(2*R**,3*S**)-3-propyloxirane (**5b**) (80mg, 0.548mmol) using method B. Flash chromatography (kieselgel, 5g, eluent ammonia (0.880 s.g., aq.) / ethanol: / dichloromethane 1:8:891 followed by 1:8:171) gave *(±)-1-[(2'R*,3'S*)-2'-methylthio-3'-hydroxyhexyl]piperidine* (60mg, 0.260mmol, 47% yield) as a yellow oil. Spectroscopic data was consistent with previous samples.

(±)-4-((2'R,3'S*)-2'-Methylthio-3'-hydroxyhexyl)morpholine* (table 3, entry 5).
Prepared from (±)-2-[(methylthio)methyl]-(2*R**,3*S**)-3-propyloxirane (**5b**) (100mg, 0.684mmol) using method B. Flash chromatography (kieselgel, 5g, eluent ammonia (0.880 s.g., aq.) / ethanol: / dichloromethane 1:8:591) gave *(±)-4-((2'R*,3'S*)-2'-methylthio-3'-hydroxyhexyl)morpholine* (70mg, 0.300mmol, 44% yield) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (t, J 6.8, 3H, C$\underline{H}_3$-6'), 1.40-1.63 (m, 4H, C$\underline{H}_2$-5' + C$\underline{H}_2$-4'), 2.11 (s, 3H, SC$\underline{H}_3$), 2.41-2.51 (m, 2H, two of C$\underline{H}_2$-3 or C$\underline{H}_2$-5), 2.56 (ddd, J 12.0, 10.0, 4.2, 1H, C$\underline{H}$-2'), 2.64-2.74 (m, 2H, remaining C$\underline{H}_2$-3 or C$\underline{H}_2$-5), 2.74 (dd, J 12.0, 10.0, 1H, one of C$\underline{H}_2$-1'), 2.84 (dd, J 10.0, 4.2, 1H, remaining C$\underline{H}_2$-1'), 3.65-3.75 (m, 3H, C$\underline{H}$-3' + C$\underline{H}_2$-2 + C$\underline{H}_2$-6); MS (EI) *m/e* 233 (M^+, 0.1), 186 (M^+-SMe, 3), 100 (100), 87 (7), 56 (9); MS (CI) *m/e* 234 (M^++1, 100); IR (thin film) 3680-3030(m), 2950 (s), 2920 (s), 2850 (m), 2820 (m), 1655 (m), 1600 (m), 1440 (s), 1170 (m), 1150 (m), 1115 (m), 1065 (m), 1025 (m), 995 (m), 955 (m), 910 (m), 860 (s), 810 (m), 795 (m), 775 (m), 745 (m); Accurate mass calculated for M^++1 $C_{11}H_{26}NO_2S$: 234.153, found (CI): 234.153.

(±)-1-[(2'R,3'S*)-2'-Phenylthio-3'-hydroxyhexyl]pyrrolidine* (table 3, entry 6).
Prepared from (±)-2-[(phenylthio)methyl]-(2*R**,3*S**)-3-propyloxirane (**5a**) (100mg, 0.482mmol) using method B. Chromatography on kieselgel (eluent ammonia (0.880 s.g., aq.) / ethanol: / dichloromethane 1:8:1791 followed by 1:8:891; 1:8:441 and 1:8:226) gave *(±)-1-[(2'R*,3'S*)-2'-phenylthio-3'-hydroxyhexyl]pyrrolidine* (45mg, 0.161mmol, 33% yield) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (t, J 7.1, 3H, C$\underline{H}_3$-6'), 1.42-1.78 (m, 7H, C$\underline{H}_2$-3 + C$\underline{H}_2$-4 + C$\underline{H}_2$-5' + one of C$\underline{H}_2$-4'), 1.88-2.01 (m, 1H, remaining C$\underline{H}_2$-4'), 2.44-2.55 (m, 2H, two of C$\underline{H}_2$-2 or C$\underline{H}_2$-5), 2.62-2.73 (m, 2H, remaining C$\underline{H}_2$-2 or C$\underline{H}_2$-5), 2.78 (dd, J 12.0, 2.7, 1H, one of C$\underline{H}_2$-1'), 3.04 (t, J 12.0, 1H, remaining C$\underline{H}_2$-1), 3.12 (td, J 12.0, 2.7, 1H, C$\underline{H}$-2'), 3.75 (td, J 12.0, 2.4, 1H, C$\underline{H}$-3'), 7.26-7.33 (m, 3H,*o*- and *p*-Ar-$\underline{H}$), 7.40 (d, J 6.3, 2H, *m*-Ar-$\underline{H}$); MS (EI) *m/e* 279 (M^+, 3), 250 (26), 155 (15), 136 (12), 123 (26), 110 (20), 105 (41), 97 (18), 84 (100), 71 (25), 69 (24), 57 (38), 55 (32), 43 (38), 41 (25); IR (thin film) 3600-3090 (m), 3070 (m), 3050 (m), 2960 (s), 2930 (m), 2875 (m), 2810 (m), 1585 (m), 1475 (s), 1455 (s), 1435 (m), 1370 (m), 1340 (m), 1135 (m), 1115 (m), 1085 (m), 1015 (m), 965 (m), 740 (s), 690 (s); accurate mass calculated for $C_{16}H_{25}NOS$: 279.166, found (EI): 279.165.

(±)-1-[(2'R,3'S*)-2'-Methylthio-3'-hydroxyhexyl]pyrrolidine* (table 3, entry 7).
Prepared from (±)-2-[(methylthio)methyl]-(2*R**,3*S**)-3-propyloxirane (**5b**) (100mg, 0.684mmol) using method B. Flash chromatography (kieselgel, 5g, eluent dichloromethane, followed successively by ammonia (0.880 s.g.,

aq.) / ethanol: / dichloromethane 1:8:891, 1:8:441 and 1:8:226) gave *(±)-1-[(2'R*,3'S*)-2'-methylthio-3'-hydroxyhexyl]pyrrolidine* (54mg, 0.249mmol, 37% yield) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (t, J 7.1, 3H, CH_3-6'), 1.40-1.95 (m, 8H, CH_2-3 + CH_2-4 + CH_2-4' + CH_2-5'), 2.10 (s, 3H, SCH_3), 2.48-2.58 (m, 3H, two of CH_2-2 or CH_2-5 + CH-2'), 2.67-2.76 (m, 2H, remaining CH_2-2 or CH_2-5), 2.80 (dd, J 12.5, 3.7, 1H, one of CH_2-1'), 3.08 (t, J 12.5, 1H, remaining CH_2-1'), 3.70 (td, J 11.1, 2.1, 1H CH-3'); MS (EI) *m/e* 217 (M^+, 10), 190 (8), 174 (72), 170 (100), 156 (11), 152 (16), 145 (42), 143 (21), 136 (24), 128 (22), 126 (23), 124 (11), 118 (12), 116 (32), 110 (25), 108 (15), 103 (59), 97 (68), 91 (23); IR (thin film) 3620 -3020(m), 2940 (s), 2910 (m), 2860 (m), 2800 (m), 1450 (s), 1430 (m), 1370 (m), 1345 (m), 1320 (m), 1285 (m), 1135 (m), 1120 (s), 1090 (m), 1020 (m), 950 (m), 900 (m), 870 (m); accurate mass calculated for $C_{11}H_{23}NOS$: 217.150, found (EI): 217.149.

(-)-Bis-N,N-((2'R,3'S)-2'-Methylthio-3'hydroxyhexyl)-2-propylamine (**9**).

Trimethylsilyl trifluoromethane sulfonate (182mg, 0.822mmol, 1.2 equivalents) was added to (-)-2-[(methylthio)methyl]-(2*R*,3*S*)-3-propyloxirane (**5b**) (100mg, 0.685mmol) in dichloromethane (2ml) at -78°C and stirred for exactly 10min.. 2-Propylamine (48mg, 0.822mmol) was added, and stirred for 4 hours at this temperature. Saturated sodium hydrogen carbonate solution (2ml) was added, the crude mixture shaken and the dichloromethane layer separated. The aqueous layer was washed with dichloromethane and the combined organic portions dried ($MgSO_4$), filtered and concentrated. Potassium carbonate (284mg, 2.06mmol) and methanol (3ml) were added and stirred at room temperature for 3 hours and the mixture then concentrated. Dichloromethane (10ml) was added, the mixture shaken and then washed with water (2x2ml). The aqueous washings were back-extracted with dichloromethane (3x5ml) and the combined organic portions dried ($MgSO_4$), filtered and concentrated. Flash chromatography (silica, 10g, eluent 3% ethyl acetate / petroleum ether, followed by 15% ethyl acetate / petroleum ether, then 30% ethyl acetate / 1% ethanol/ petroleum ether) gave *(-)-Bis-N,N-((2'R,3'S)-2'-methylthio-3'hydroxyhexyl)-2-propylamine* (23mg, 0.051mmol, 15% yield) as a yellow oil: ^{1}H NMR (300MHz, $CDCl_3$) δ 0.92-0.99 (m, 9H, 2 x CH_3-6' + three of CH_3-1 or CH_3-3), 1.13 (d, J 6.9, 3H, remaining CH_3-1 or CH_3-3), 1.32-1.75 (m, 8H, 2 x CH_2-4 + CH_2-5), 2.13 (s, 6H, 2 x SCH_3), 2.62-2.71 (m, 4H, 2 x CH-2' + 2 x one of CH_2-1'), 2.87 (dd, J 15.3, 10.5, 2H, 2 x remaining CH-1'), 3.15 (quintet, J 6.9, 1H, CH_2-2), 3.76 (ddd, J 7.5, 5.8, 3.0, 2H, 2 x CH_2-3'); MS (EI) *m/e* 351 (0.5, M^+), 350 (2, M^+-1), 218 (100), 170 (22), 147 (63), 116 (17), 99 (44), 86 (19), 81 (12), 74 (30), 72 (39), 61 (85), 57 (16), 55 (27), 43 (32), 41 (20), 32 (14); IR (thin film) 3630-3030 (m), 2960 (s), 2930 (s), 2870 (m), 1455 (s), 1430 (m), 1385 (m), 1365 (m), 1315 (m), 1160 (m), 1125 (m), 1105 (m), 1085 (m), 1070 (m), 1025 (m), 1005 (m), 955 (m), 845 (m), 745 (m); accurate mass calculated for M^+ $C_{17}H_{35}NO_2S_2$: 351.227; found (EI): 351.225; $[\alpha]_D^{20}$ -40.8° (*c* 1.02, ethanol).

Table 4: Use of imines as synthetic equivalents for the selective monoalkylation of primary amines.

Typical procedure:

(±)-N-[(2'R,3'S*)-2'-Methylthio-3'-hydroxyhexyl]-2-propylamine* (table 4, entry 2).

Trimethylsilyl trifluoromethanesulfonate (182mg, 0.822mmol) was added to a solution of (±)-2-[(methylthio)methyl]-(2*R**,3*S**)-3-propyloxirane (**5b**) (100mg, 0.684mmol) in dichloromethane (2ml) at -78°C. After stirring for 10 minutes, N-*iso*-propyl anisylidene imine[30] (242mg, 1.37mmol) was added and stirring continued for a further 10 minutes at this temperature and for 12 hours at 0°C. Potassium carbonate (142 mg, 1.03mmol) and methanol (3ml) was added and stirring continued for 2 hours at room temperature. The reaction mixture was concentrated, then redissolved in dichloromethane (10ml) and washed with water (2 x 2ml). The aqueous washings were back-extracted with dichloromethane (4 x 5 ml) and the combined dichloromethane portions dried ($MgSO_4$), filtered and concentrated. The mixture was stirred with ammonia (aqueous, s.g. 0.880) / ethanol / dichloromethane, 1:8:91) for 1 hour at room temperature, then concentrated. Flash chromatography (magnesium silicate, 5g, eluent ammonia (aqueous, s.g. 0.880) / ethanol / dichloromethane, 1:8:8991 then 1:8:891) gave *(±)-N-[(2'S*,3'S*)-2'-methylthio-3'-hydroxyhexyl]-2-propylamine* (89mg, 0.434mmol, 63% yield) as a yellow oil: ^{1}H NMR (300MHz, $CDCl_3$) δ 0.94 (t, J 7.2, 3H, CH_3-6'), 1.09 (d, J 7.1, 6H, CH_3-1 + CH_3-3), 1.35-1.65 (m, 4H, CH_2CH_2), 2.12 (s, 3H, SCH_3), 2.57 (ddd, J 11.8, 7.6, 5.6, 1H, CH-2'), 2.81 (quintet, J 7.1, 1H, CH-2), 2.92 (dd, J 14.3, 7.6, 1H, one of CH_2-1'), 3.10 (dd, J 14.3, 5.6, 1H, remaining

$C\underline{H}_2$-1'), 3.75 (ddd, J 11.8, 7.7, 5.0, 1H, C<u>H</u>-3'); MS (CI) *m/e* 206 (M^++1, 100); IR thin film 2960 (m), 2940 (m), 1450 (m), 1280 (m), 1160 (m); Accurate mass calculated for M^++1 $C_{10}H_{24}NOS$: 206.193, found: 206.192.

Analogous procedures using *N*-iso-propyl benzylidene imine[29] (table 4, entry 1) and *N*-iso-propyl *p*-acetylidene imine[30] (table 4, entry 3) gave the same product in 37 and 70% yields respectively.

(+)-N-[(2'R,3'R)-2'-Phenylthio-3'-hydroxyhexyl]-2-propylamine (table 4, entry 4).
Trimethylsilyl trifluoromethanesulfonate (128mg, 0.577mmol) was added to a solution of (+)-2-[(phenylthio)methyl]-(2*R*,3*R*)-3-propyloxirane (**5c**) (100mg 0.481mmol) in dichloromethane (2ml) at -78°C. After stirring for 10 minutes, N-*iso*-propyl anisylidene imine (170mg, 0.962mmol) was added and stirring continued for a further 10 minutes at this temperature and for 2 days at 0°C. Potassium carbonate (199 mg, 1.44mmol) and methanol (3ml) was added and stirring continued for 3 hours at room temperature. The reaction mixture was concentrated, then redissolved in dichloromethane (10ml) and washed with water (2 x 2ml). The aqueous washings were back-extracted with dichloromethane (4 x 5 ml) and the combined dichloromethane portions dried ($MgSO_4$), filtered and concentrated. Flash chromatography (magnesium silicate, 10g, eluent ammonia (aqueous, s.g. 0.880) / ethanol / dichloromethane, 1:8:8991 then 1:8:891) gave *(+)-N-[(2'R,3'R)-2'-phenylthio-3'-hydroxyhexyl]-2-propylamine* (74mg, 0.276mmol, 57% yield) as a yellow oil: ^{1}H NMR (300MHz, $CDCl_3$), δ 0.94 (t, J 8.6, 3H, $C\underline{H}_3$-6'), 1.03 (apparent t, J 6.7, 6H, $C\underline{H}_3$-1 + $C\underline{H}_3$-3), 1.30-1.82 (m, 4H, $C\underline{H}_2$-4 + $C\underline{H}_2$-5), 2.74 (q, J 7.4, 1H, C<u>H</u>-2), 2.83 (dd, J 15.0, 5.4, 1H, one of $C\underline{H}_2$-1'), 3.09 (dd, J 15.0, 5.4, 1H, remaining $C\underline{H}_2$-1'), 3.30 (td, J 5.4, 2.7, 1H, C<u>H</u>-2'), 4.01 (dt, J 6.7, 2.7, 1H, C<u>H</u>-3'), 7.20-7.34 (m, 3H, *o*- and *p*-Ar-<u>H</u>), 7.43 (dd, J 6.4, 2.3 *m*-Ar-<u>H</u>); MS (CI) *m/e* 268 (M^++1, 100); IR (thin film) 3060 (m), 2960 (m), 2865 (m), 1580 (m), 1450 (m), 1120 (m), 740 (m), 690 (m); Accurate mass calculated for M^++1 $C_{15}H_{26}NOS$: 268.174; found (CI): 268.174.

(+)-N-[(2'R,3'R)-2'-Phenylthio-3'-trimethylsilyloxyhexyl]aniline (table 4, entry 5).
Trimethylsilyl trifluoromethanesulfonate (128mg, 0.577mmol) was added to a solution of (+)-2-[(phenylthio)methyl]-(2*R*,3*R*)-3-propyloxirane (**5c**) (100mg, 0.481mmol) in dichloromethane (2ml) at -78°C. After stirring for 10 minutes, N-phenyl anisylidene imine (132mg, 0.625mol) was added and stirring continued for a further 10 minutes at this temperature and for 2 days at 0°C. Aqueous, saturated potassium carbonate (3ml) was added and stirring continued for 2 hours at 0°C. The layers were separated and the aqueous layer back-extracted with dichloromethane (4 x 5 ml). The combined dichloromethane portions were dried ($MgSO_4$), filtered and concentrated. Flash chromatography on 10g silica (eluent: petroleum ether followed by 1% ethyl acetate / petroleum ether) gave *(+)-N-[(2'R,3'R)-2'-phenylthio-3'-trimethylsilyloxyhexyl]aniline* (119mg, 0.319mmol, 66% yield) as a yellow oil: ^{1}H NMR (300MHz, $CDCl_3$), δ 0.04 (s, 9H, $(C\underline{H}_3)_3Si$), 0.92 (t, J 7.2, 3H, $C\underline{H}_3$-6'), 1.12-1.57 (m, 3H, $C\underline{H}_2$-5' + one of $C\underline{H}_2$-4'), 1.69-1.84 (m, 1H, remaining $C\underline{H}_2$-4'), 3.19 (dd, J 12.2, 7.7, 1H, one of $C\underline{H}_2$-1'),3.36 (ddd, J 7.7, 5.6, 2.8, 1H, C<u>H</u>-2'), 3.61 (dd, J 12.2, 5.6, 1H, remaining $C\underline{H}_2$-1'), 3.88 (dt, J 8.8, 2.8, 1H, C<u>H</u>-3'), 6.57 (d, J 8.3, 2H, *o*- Ar-<u>H</u> on nitrogen), 6.70 (t, J 7.2, 1H, *p*- Ar-<u>H</u> on nitrogen), 7.15 (dd, J 8.3, 7.2, 2H, *m*- Ar-<u>H</u> on nitrogen), 7.24-7.35 (m, 3H, *o*- and *p*- Ar-<u>H</u> on sulfur), 7.42 (dd, J 8.8, 2.5 *m*- Ar-<u>H</u> on sulfur); MS (EI) *m/e* 373 (M^+) (15), 178 (100), 145 (24), 106 (80) 77 (20), 73 (48); IR (thin film) 3580-3170 (m, br, N-H), 3060 (w, Ar C-H), 3040 (w, Ar C-H), 2980 (s, alkyl C-H), 2940 (m, alkyl C-H), 2880 (m, alkyl C-H), 1600 (s, Ar C-C), 1500 (s, Ar C-C), 1475 (m,),1320 (m), 1250 (s), 1090 (m), 1060 (m), 1035 (m), 995 (m), 840 (s), 745 (s), 690 (s); accurate mass calculated for M^+ $C_{31}H_{31}NOSSi$: 373.190: found (EI): 373.190; $[\alpha]_D^{20}$ +22.6° (*c* 1.33, ethanol).

(+)-N-(2R,3R)-[2-Phenylthio-3-hydroxyhexyl]benzylamine (table 4, entry 6).
Trimethylsilyl trifluoromethanesulfonate (128mg, 0.577mmol) was added to a solution of (+)-2-[(phenylthio)methyl]-(2*R*,3*R*)-3-propyloxirane (**5c**) (100mg, 0.481mmol) in dichloromethane (2ml) at -78°C. After stirring for 10 minutes, N-benzyl anisylidene imine (141mg, 0.625mmol) was added and stirring continued for a further 10 minutes at this temperature and for 36 hours at 0°C. Aqueous, saturated potassium carbonate (3ml) was added and stirring continued for 3 hours at room temperature. The layers were separated and the aqueous layer back-extracted with dichloromethane (4 x 5 ml). The combined dichloromethane portions were dried ($MgSO_4$), filtered and concentrated. Flash chromatography (silica, 10g, eluent 1% ethyl acetate / petroleum ether) gave *(+)-N-(2R,3R)-[2-phenylthio-3-hydroxyhexyl]benzylamine* (70mg 0.222mmol, 46% yield) as a

yellow oil: ^{1}H NMR (300MHz, $CDCl_3$), δ 0.94 (t, J 7.5, 3H, $C\underline{H}_3CH_2$), 1.25-1.76 (m, 4H, $C\underline{H}_2C\underline{H}_2$), 2.84 (dd, J 12.0, 3.6, 1H, one of $C\underline{H}_2$-1'), 3.07 (dd, J 12.0, 4.3, 1H, remaining $C\underline{H}_2$-1'), 3.30 (ddd, J 5.0, 4.3, 3.6, 1H, C<u>H</u>-2'), 3.78 (s, 2H, $C\underline{H}_2C_6H_5$), 3.99 (ddd, J 7.5, 5.0, 3.0, 1H, C<u>H</u>-3), 7.22-7.40 (m, 10H, Ar<u>H</u>); MS (EI) *m/e* 316 (M^++1, 45), 315 (M^+, 9), 206 (M^+-SPh, 13), 178 (92), 149 (62), 136 (58), 123 (36), 120 (90), 109 (46), 91 (100), 77 (39), 65 (60), 57 (30), 55 (34), 51 (29), 45 (26), 43 (49), 41 (40); IR (thin film) 3670-3100 (m), 3050 (w), 3030 (w), 2930 (s), 2860 (m), 1580 (m), 1475 (m), 1460 (s), 1450 (s), 1440 (s), 1115 (m), 1075 (m), 1020 (m), 735 (s), 695 (s); Accurate mass caculated for M^++1 $C_{19}H_{26}NOS$: 316.174; found 316 173; $[\alpha]_D^{20}$ +34.3° (*c* 1.10, ethanol).

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References and Notes

1. Sharpless, K.B.; Exon, C.M.; Regenye, R. *Org. Synth.*, **1984**, *63*, 66-78; Katsuki, T.; Sharpless, K.B. *J. Am. Chem. Soc.*, **1980**, *102*, 5974-5976; Hill, J.G.; Finn, M.G.; Sharpless, K.B. *Asymmetric Synthesis*, ed. J.D. Morrison, Academic Press, New York, 1985, Vol. 5.
2. Pfenninger, A. *Synthesis*, **1986**, 89-116; Rossiter, B.E. *Asymmetric Synthesis*, ed. Morrison, J.D., Academic Press, New York. 1985, Vol. 5; Johnson, R.A.; Sharpless, K.B. in *Comprehensive Organic Synthesis*, ed. Trost, B.M., Pergamon Press, Oxford, 1991, vol. 7, chap. 3.2, pp. 389-436.
3. Westwell, A.D.; Thornton-Pett, M.; Rayner, C.M. *J. Chem. Soc., Perkin Trans. 1*, **1995**, 847-859 and refs. cited therein.
4. For other reports of 2,3-epoxy sulfide derivatives see: Fruchier, A.; Morangues, V.; Petrus, C.; Petrus, F. *Bull. Chem. Soc. France*, **1984**, *II*, 173-182; Fujisawa, T.; Itoh, T.; Nakai, M.; Sato, T. *Tetrahedron Lett.*, **1985**, *26*, 771-774; Itoh, T.; Yoshinaka, A.; Sato, T.; Fujisawa, T. *Chemistry Lett.*, **1985**, 1679-1680; Apparao, S.; Schmidt, R.R. *Synthesis*, **1987**, 896-899; Gu, X.P.; Ikeda, I.; Okahara, M. *Bull. Chem. Soc. Japan*, **1987**, *60*, 667-672; Kalugin, V.E.; Litvinov, V.P. *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1991**, *18*, 2829-2832; Niyazymbetov, M.E.; Konyushkin, L.D.; Niyazymbetova, Z.I.; Kalugin, V.E.; Litvinov, V.P.; Petrosyan, V.A. *Tetrahedron Lett.*, **1991**, *32*, 1099-1102; Takano, S.; Sugihara, Y.; Ogasawara, K. *Synlett*, **1992**, 668-670; Takano, S.; Sugihara, Y.; Ogasawara, K. *Tetrahedron Lett.*, **1993**, *34*, 845-848.
5. Liu, Q.; Simms, M.J.; Boden, N.; Rayner, C.M. *J. Chem. Soc., Perkin Trans. 1*, **1994**, 1363-1366.
6. Liu, Q.; Marchington, A.P.; Boden, N.; Rayner, C.M. *Synlett*, **1995**, 1037-1039.
7. Preliminary communications: a) Gill, D.M.; Pegg, N.A.; Rayner, C.M. *J. Chem. Soc., Perkin Trans. 1*, **1993**, 1371-1372; b) *idem*, *Tetrahedron Lett.*, **1995**, *36*, 8327-8330; c) *idem*, *Synlett*, in press.
8. Smit, W.A.; Zefirov, N.S; Bodrikov, I.V.; Krimer, M.Z. *Acc. Chem. Res.*, **1979**, *12*, 282-288.
9. Rayner, C. M. in "Organosulfur Chemistry Series", ed. Page, P.C.B., Pergamon Press, 1995, chapter 3; see also Capozzi, G.; Modena, G.; Pasquato, L. in "The chemistry of sulphenic acids and their derivatives", ed. Patai, S., J. Wiley, Chichester, 1990, chapter 10.
10. Coldham, I.; Warren, S. *J. Chem. Soc., Perkin Trans. 1*, **1993**, 1637-1656; Sansbury, F.H.; Warren, S. *Tetrahedron Lett.*, **1992**, *33*, 539-542; Aggarwal, V.K.; Coldham, I.; McIntyre, S.; Warren, S. *J. Chem. Soc., Perkin Trans. I*, **1991**, 451-460; Hall, D.; Sevin, A.-F.; Warren, S. *Tetrahedron Lett.*, **1991**, *32*, 7123-7126; Chibale, K.; Warren, S. *Tetrahedron Lett.*, **1991**, *32*, 6645-6648.
11. Williams, D.R.; Phillips, J.G. *Tetrahedron*, **1986**, *42*, 3013-3019; Trost, B.M.; Shibata, T. *J. Am. Chem. Soc.*, **1982**, *104*, 3225-3228; Trost, B.M.; Shibata, T.; Martin, S.J. *ibid*, **1982**, *104*, 3228-3230; see also ref. 9 and references cited therein.
12. Derzhinskii, A.R.; Konyushkin, L.D.; Lutsenko, A.I. *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1984**, *11*, 2652; Miyauchi, H.; Nakamura, T.; Ohashi, N. *Bull Chem. Soc. Japan*, **1995**, *68*, 1731-1737.
13 For example by Pummerer rearrangement of the corresponding sulfoxide and hydrolysis, see: De Lucchi, O.; Miotti, U.; Modena, G. *Organic Reactions*, **1990**, *40*, 157-405.
14 Corrie, J.E.T.; Hlubucek, J.R.; Lowe, G. *J. Chem. Soc., Perkin Trans. I*, **1977**, 1421-1425; Sakakibara, S.; Shimonishi, Y.; Kishida, Y.; Okada, M.; Sugihara, H. *Bull. Chem. Soc. Japan*, **1967**, *40*, 2164-2167.
15 Henkel, J.G.; Amato, G.S. *J. Med. Chem.*, **1988**, *31*, 1279-1282; see also: Reetz, M. T.; Seitz, T. *Angew. Chem. Int. Ed. Engl.*, **1987**, *26*, 1028.

16 Sharpless, K.B.; Verhoeven, T.R. "Selections from the Aldrichimica Acta", Aldrich Chemical Company Inc., **1984**, 201-212; *Aldrichimica Acta*, **1979**, *12*, 63-74.
17 Nakagawa, I.; Hata, T. *Tetrahedron Lett.*, **1975**, 1409-1412.
18. Payne, G.B. *J. Org. Chem.*, **1962**, *27*, 3819-3822.
19. Page, P.C.B.; Rayner, C.M.; Sutherland, I.O. *J. Chem. Soc., Perkin Trans. I*, **1990**, 1375-1382 and references cited therein.
20 See for example: Oki, M.; Nakanishi, W.; Fukunaga, M.; Smith, G.D.; Duax, W.L.; Osawa, Y. *Chemistry Lett.*, **1975**, 1277-1280. See also ref. 9.
21 Toshimitsu, A.; Hirosawa, C.; Tanimoto, S. *Tetrahedron Lett.*, **1991**, *32*, 4317-4320.
22 Archer, N.J.; Rayner, C.M.; Bell, D.; Miller, D. *Synlett*, **1994**, 617-619; see also: Lucchini, V.; Modena, G.; Pasquato, L. *J. Chem. Soc., Chem. Commun.*, **1994**, 1565-1566.
23 Vorbruggen, H.; Krolikiewicz, K.; Bennua, B. *Chem. Ber.*, **1981**, *114*, 1234-1255; Birkofer, L.; Ritter, A.; Kuhlthau, H.-P. *Chem. Ber.*, **1964**, *97*, 934-945.
24 Kulkarni, S.; Abdul-Baky, S.; Le Quesne, P.W.; Vouros, P. *Steroids*, **1989**, *53*, 131-147.
25 Yoder, C.H.; Copenhafer, W.C.; DuBeshter, B. *J. Am. Chem. Soc.*, **1974**, *96*, 4283; Birkofer, L.; Ritter, A. *Angew. Chem. Int. Edn. Engl.*, **1965**, *4*, 417-429; Knapp, S.; Rodriques, K.E. *Tetrahedron Lett.*, **1985**, *26*, 1803-1806.
26 Combret, J.C.; Klein, J.L.; Mouslouhouddine, M. *Synthesis*, **1984**, 493-495.
27 Djuric, S. ; Venit, J.; Magnus, P. *Tetrahedron Lett.*, **1981**, *22*, 1787-1990.
28 Lucier, J.J.; Harris, A.D.; Korosec, P.S. *Org. Synth., Coll. Vol. 5*, **1973**, 736-739; Wawzonek, S.; McKillip, W.; Peterson, C.J. *Org. Synth., Coll. Vol. 5*, **1973**, 758-761.
29 a) Lutz, R.E.; Bailey, P.S.; Rowlett Jr., R.J.; Wilson, J.W.; Allison, R.K.; Clark, M.T.; Leake, N.H.; Jordan, R.H.; Keller, R.; Nicodemus, K.C. *J. Org. Chem.*, **1947**, *12*, 760-766; b) Steck, E.A.; Hallock, L.L.; Suter, C.M. *J. Am. Chem. Soc.*, **1948**, *70*, 4063-4065; see also: Stork, G.; Leong, A.Y.W.; Touzin, A.M. *J. Org. Chem.*, **1976**, *41*, 3491-3493.
30 Ebara, N. *Bull. Chem. Soc. Japan*, **1961**, *34*, 1151-1158.
31 Snyder, H.R.; Matteson, D.S. *J. Am. Chem. Soc.*, **1957**, *79*, 2217-2221.
32 Anselmino, O. *Berichte*, **1907**, *40*, 3465-3474; Roe, A.; Montgomery, J.A. *J. Am. Chem. Soc.*, **1953**,*75*, 910-912.
33 Ingold, C.K.; Shoppee, C.W. *J. Chem. Soc.*, **1929**, 1199-1204; Frohlich, E.; Wunderkind, E. *Berichte*, **1907**, *40*, 1001-1009; see also ref. 32.
34. Leonard, J.; Lygo, B.; Procter, G. *Advanced Practical Chemistry*, Blackie, 1990.
35. Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*, Pergamon, 1980.
36. Mori, K.; Nakazano, Y. *Tetrahedron*, **1986**, *42*, 6459-6464.
37. Nishimura, T.; Shimizu, B.; Iwai, I. *Chem. Pharm. Bull.*, **1963**, *11*, 1470-1472.
38. Mittendorf, J.; Hiemstra, H.; Speckamp, W.N. *Tetrahedron*, 1990, **46**, 4049-4062.

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