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PAPER

Synthesis of chiral sulfoximines derived from 3-aminoquinazolinones and their catalysis of enantioselective diethylzinc addition to aldehydes†

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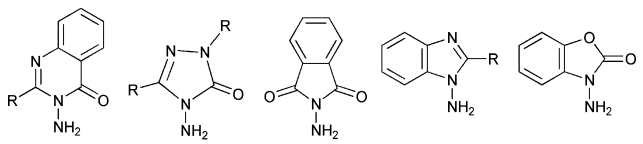
A series of sulfoxides were sulfoximinated using oxidative addition of 3-aminoquinazolinones by lead tetraacetate in the presence of hexamethyldisilazane. They were applied for the first time in catalytic enantioselective addition to aromatic aldehydes with a product enantiopurity (ee) of 92% in the case of 2-methoxybenzaldehyde.

1. Introduction

Oxidation of the family of *N*-aminoheterocycles **1–5**, with lead tetraacetate (LTA) in the presence of electron-rich and electron-deficient alkenes results in aziridines, often in excellent yields[1] (Scheme 1). Among these *N*-aminoheterocycles **1–5**, 3-aminoquinazolinones **1** (QNH_2) have been the most extensively used.



1 **2** **3** **4** **5**

Scheme 1

Quinazolinones and quinazolines are also present in naturally occurring alkaloids and play a crucial role in biological activity.[2–5] Reagent[6–10] or substrate-controlled[11] diastereoselective aziridination of alkenes can be accomplished by incorporation of a chiral centre into the 2-position of quinazolinone **1** or into the alkene. We have recently reported[12] that aziridination of allylic alcohols **6** using 2-ethyl-3-acetoxyaminoquinazolinone **7** (Q^1NHOAc) as the aziridinating agent, gives aziridine diastereoselectivities of up to >99 : 1 (Scheme 2). This high *syn*-diastereoselectivity was presumed to result from hydrogen bonding between the hydrogen of the hydroxyl group and the oxygen of quinazolinone carbonyl group as in **8**.

Sulfoximines are of considerable interest since they are substrates for conversion into biologically active molecules such as alkaloids[13–19] and amino acids.[20–23] Their chirality makes them potentially useful in stereoselective synthesis[24–29] and new synthetic applications are currently being developed.[20,27,30–36]; of particular interest is their bioactivity as tumour metastasis inhibitors.[37–39] This growing interest is also focussed on their significant potential in asymmetric synthesis[24–29] and new synthetic applications are currently being developed.[20,27,30–36] Bolm and Okamura have studied the catalytic applications of a new class of sulfoximine ligands and their *N*-acylated derivatives.[30,31,40] A synthetically valuable NH-sulfoximines procedure has been developed by Yudin by electrochemical sulfoximination of sulfoxide using *N*-aminophthalimide followed by cleavage of the N–N bond.[41]

In 1996, Bolm's group introduced sulfoximine as an enantiopure ligand in a Pd complex-catalyzed asymmetric allylation reaction, yielding the product with 73% ee.[42] Subsequently, Bolm and others[43] developed a series of enantiopure sulfoximines **10–13** (Scheme 3) for use in Diels–Alder,[28,44] carbonyl-ene,[45,46] asymmetric hydrogenation,[27,47] Mukaiyama aldol,[26,48,49] and trimetylsilylcyanation of aldehyde[50] reactions as well as enantioselective conjugate addition of diethylzinc to chalcones.[51]

In this paper we describe, in detail, the imination of sulfoxides using 3-aminoquinazolinones and their catalysis of (enantioselective) diethylzinc addition to aldehydes.

2. Results and Discussions

We recently communicated that in sulfoximination of sulfoxide using Q^1NHOAc **7**, yields are improved by the presence of hexamethyldisilazane (HMDS)[52] (Scheme 4). Initially, DMSO was converted into sulfoximine at –18 °C in only 35% yield using an equimolar molar of Q^1NHOAc **7,** as well as QH **6** which is a by-product in the aziridination of electron-deficient alkenes.[11,53]

In this sulfoximination, competitive decomposition of Q^1NHOAc **7** (stable at <0 °C) is a consequence of the acetic acid (AcOH) produced in the acetoxylation of 3-aminoquinazolinone

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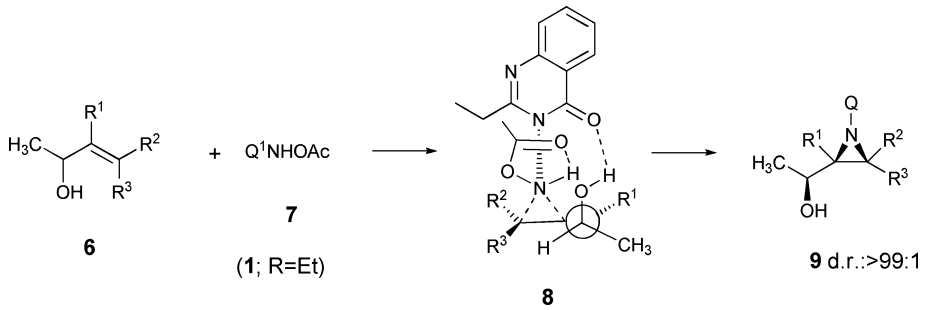
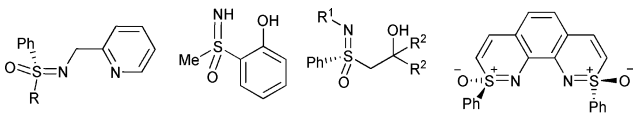
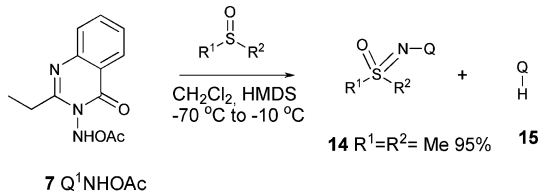


Scheme 2

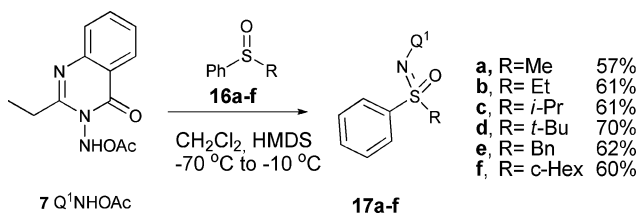


Scheme 3



Scheme 4

1 (R = Et) and in the sulfoximination steps. Using HMDS (2 eq) to scavenge AcOH, increasing to 2 eq the ratio of DMSO (2 eq) and lowering the reaction temperature to –70 °C then finishing the reaction at –10 °C gave the product **14** as crystalline solid in 95% yield (see General procedure in Experimental section). A number of alkyl phenyl sulfoxides were then iminated (Scheme 5) with is modified procedure described above using Q[1]NHOAc **7** and giving the sulfoximines shown up to 70% isolated yields.



Scheme 5

The advantage of using 3-aminoquinazolinones **1** over *N*-aminoheterocycles **2–5** in aziridination of alkenes is the ease of incorporation of a chiral centre into its 2-position, which makes available aziridines in enantiopure form.[1] For this reason, and as part of our program devoted to the study of this new sulfoximination process, we were keen on devising a diastereoselective version of this reaction.

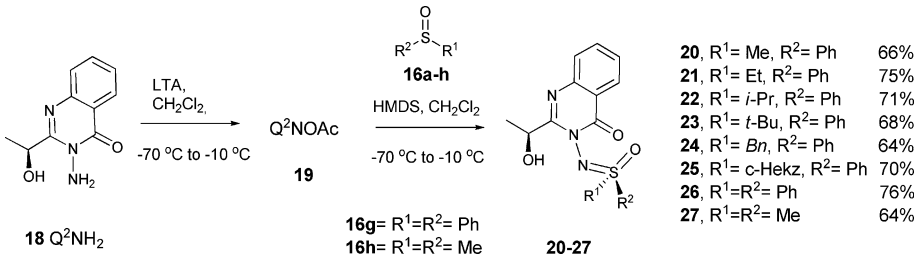
Thus, imination of methyl phenyl sulfoxide **16a** with **19** gave the product **20** in 66% yield (Scheme 6). An NMR spectrum of the crude product showed a 1.3 : 1 ratio of sulfoximine diastereoisomers (**20a** and **20b**) from comparison of methyl signal intensity at the sulfur chiral centre at δ 3.36 and 3.32 ppm respectively. Unreacted methyl phenyl sulfoxide **16a** from this reaction indicated a predominance of the (*R*)-sulfoxide by HPLC analysis using chiral column (Chiralcel OD-H). Hence the absolute configuration of the major sulfoximine (**20a**) diastereoisomer is *S* as displayed in Scheme 6. As was previously known, reagent-controlled diastereoselective aziridination of styrene with (*S*)-*tert*-leucine derived 3-aminoquinazolinone **30** (Q^3NH_2) gave a 1 : 1.5 ratio of aziridine diastereoisomers. However, when this aziridination was repeated in the presence of $Ti(OPr^i)_4$, this ratio of aziridines is >50 : 1. The same enhanced diastereoselectivities were also obtained for butadiene and indene derived aziridines.[54,55]

Repetition of our sulfoximination reaction using $Ti(OPr^i)_4$ present, however gave no enhancement of diastereoselectivity (d.r. 1 : 1) from comparison of the same signals previously compared in the ^{1}H NMR spectrum of the sulfoximine. Separation of minor **20a** (R_f 0.2) and major (R_f 0.12) sulfoximine **20b** diastereoisomers as colourless oils was accomplished by chromatography over silica. Alkyl phenyl sulfoxides 16b–h were then iminated under the same reaction conditions and the diastereoisomer ratios of the resulting sulfoximines measured by NMR but in every case a 1 : 1 ratio was obtained.

Each of the crude diastereoisomeric sulfoximines was then chromatographed over silica and separated as single oily or solid diastereoisomers except **22** and **25**. Enrichment of the phenylcyclohexylsulfoximine **25** to a 95 : 5 ratio of diastereoisomers was achieved by crystallisation from ethanol. A single crystal of sulfoximine diastereoisomer **23a** suitable for X-ray crystal structure determination was also prepared by crystallisation from ethanol. The compound **23a** crystallizes in the monoclinic non-centrosymmetric chiral space group $P2_1$ with four molecules in the unit cell. It has the configuration shown in Fig. 1, which is the (*S*)-configuration at the chiral center (related to the asymmetric C atom at C19 and C19′) and related *R*-chiral sulfoxides was assigned [Flack parameter *x*: –0.012(0.06)].

Absolute configuration of *N*-phthalimidosulfoximines and related (*S*)-chiral sulfoxides has previously been assigned by exciton-coupled circular dichroism.[56] Sulfoximines prepared from *N*-aminophthalimide and sulfoxides are believed to be formed with retention of configuration at sulfur.

We prepared enantiopure (*S*)-*t*-butyl phenyl sulfoxide **23** by the procedure of Kagan[57] and iminated using Q^2NHOAc **19** to give sulfoximine **23b**. The configuration at sulfur was retained in the sulfoximine product which is in agreement with the known configuration of the authentic samples as has been shown previously. The mechanism shown in Fig. 2 for Q^2NHOAc **19** imination of sulfoxides is analogous to the Bartlett mechanism for



Scheme 6

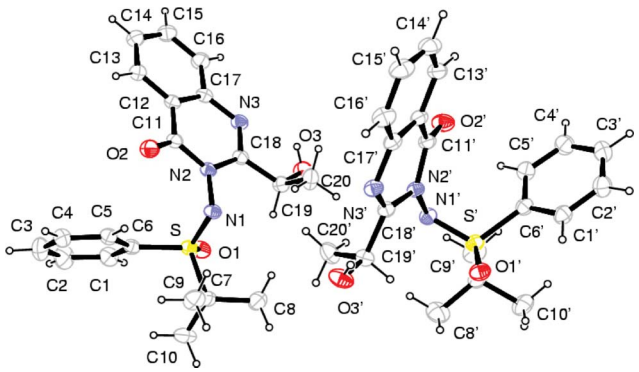


Fig. 1 An ORTEP drawing of the molecule **23a**. The asymmetric unit contains two independent molecules with nearly identical geometries. Displacement ellipsoids are drawn at the 40% probability level.

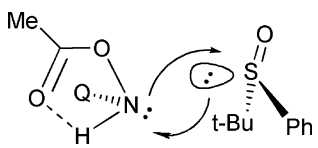


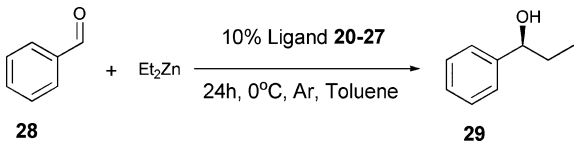
Fig. 2

mCPBA epoxidation of alkenes or for aziridination of electron rich alkenes *e.g.* styrene by Q^2NHOAc **19**.[1,7]

To examine the performance of sulfoximines **20–27** as chiral ligands in catalytic enantioselective addition of alkylzinc reagents to aldehydes, we chose the addition of Et_2Zn to benzaldehyde **28** as a reference reaction (Scheme 7). The reaction was attempted at the temperature of 0 °C, 10% ligand, 2 eq of Et_2Zn and toluene as solvent and the results are shown in Table 1.

Table 1 Addition of diethylzinc to benzaldehyde in the presence of ligand **20–27**

Entry	Sulfoximine	ee (%)	Yield (%)	Configuration
1	**20a** S,S_S	42	56	*S*
2	**20b** S,R_S	50	94	*S*
3	**21a**	31	81	*S*
4	**21b**	47	94	*S*
5	**22**	58	53	*S*
6	**23a** S,R_S	45	99	*S*
7	**23b** S,S_S	62	99	*S*
8	**24a**	36	89	*S*
9	**24b**	44	91	*S*
10	**25**	57	53	*S*
11	**26**	61	99	*S*
12	**27**	24	85	*S*



Scheme 7

Examination of Table 1 shows the formation of enantiomerically enriched product 1-phenyl-1-propanol **29** in the presence of sulfoximine catalysts **23b**, and **26** in 62% and 61% ee respectively and in excellent yields (99%). The reaction when carried out using diastereomeric mixture (1 : 1) of sulfoximine **22** or of sulfoximine **25** (19 : 1), displayed almost the same enantioselection (58% and 57% ees).

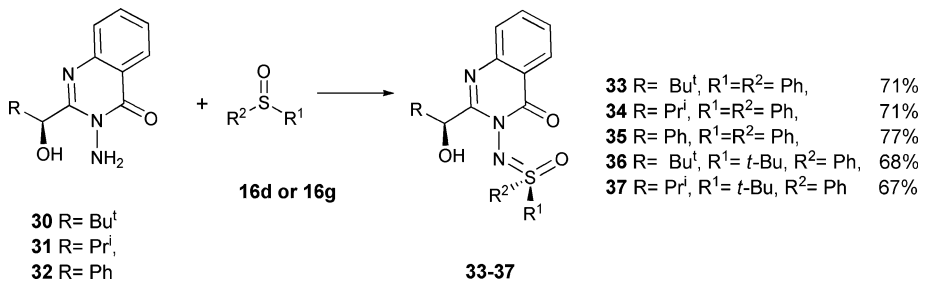
Different and better differentiated substituents on the chiral centre on the 2-position of the quinazolinones could give better diastereoselectivities for imination of sulfoxides and enantioselectivities in catalytic C–C bond formations. For this reason, we repeated the imination process of *t*-butyl phenyl sulfoxide and diphenyl sulfoxide using 3-aminoquinazolinones **30–32**[55,58] (Scheme 8). In each case, *t*-butyl phenyl sulfoxide derived sulfoximines **36** and **37** contained 1 : 1 diastereoisomeric mixtures from analysis of their ^{1}H NMR spectra. Repetition of the catalytic enantioselective reaction as in Scheme 7 reveals slightly higher enantioselectivities using (*S*)-valin derived quinazolinone sulfoximine ligands **34** and **37b** (68% ee Table 2, Entries 2 and 7). There was no observation of enantioselection in formation of the corresponding alcohol, when mandelic acid derived quinazolinone sulfoximine **35** was used as ligand (Entry 3). Because of its easy preparation and purification, ligand **34** was used in subsequent variations of reaction conditions including the influence of the Lewis acid $Ti(OPr^i)_4$, solvent, temperature as well as ligand percentage.

Changing the reaction condition in presence of $Ti(OPr^i)_4$ (Entry 8) gave a lower ee. When the temperature was lowered to –20 °C (Entry 9), the reaction proceeded with good yield and with an ee somewhat higher than at 0 °C. The lowest enantioselectivity (18% ee) and product yield (3%) was achieved in the presence of THF as solvent. When the reaction was performed in Et_2O and the reaction temperature lowered to –40 °C, we obtained the best enantioselection (90% ee Entry 15). Increasing the temperature to ambient had adverse effects on the enantioselectivity (21% ee) (Entry 16). Decreasing to temperature to –70 °C gave a good enantioselectivity (89% ee) but the lowest product yield (21%) (Entry 17). Altering the mol equivalent of Et_2Zn (Entry 18 and 19) or of sulfoximine (Entry 20 and 21) gave no improvements in enantioselectivity.

Table 2 Et_2Zn addition benzaldehyde catalysed by **33–37**

Entry	Sulfoximine	Lewis acid	Temp. °C	Solvent	Ee (%)	Yield (%)	Configuration
1	**33**	—	0	Toluene	46	99	*S*
2	**34**	—	0	Toluene	68	97	*S*
3	**35**	—	0	Toluene	0	99	*S*
4	**36a**	—	0	Toluene	44	98	*R*
5	**36b**	—	0	Toluene	48	98	*S*
6	**37a**	—	0	Toluene	50	96	*S*
7	**37b**	—	0	Toluene	68	72	*S*
8	**34**	$Ti(OPi)_4$	0	Toluene	51	94	*S*
9	**34**	$Ti(OPi)_4$	–20	Toluene	77	92	*S*
10	**34**	$Ti(OPi)_4$	–20	Hexane	76	99	*S*
11	**34**	$Ti(OPi)_4$	–20	Et_2O	80	83	*S*
12	**34**	$Ti(OPi)_4$	–20	THF	18	3	*S*
13	**34**	$Ti(OPi)_4$	–20	CH_2Cl_2	61	57	*S*
14	**34**	$Ti(OPi)_4$	–20	Dioxane	72	85	*S*
15	**34**	$Ti(OPi)_4$	–40	Et_2O	90	67	*S*
16	**34**	$Ti(OPi)_4$	rt	Et_2O	21	98	*S*
17	**34**	$Ti(OPi)_4$	–70	Et_2O	89	11	*S*
18	**34**[a]	$Ti(OPi)_4$	–40	Et_2O	80	70	*S*
19	**34**[b]	$Ti(OPi)_4$	–40	Et_2O	90	52	*S*
20	**34**[c]	$Ti(OPi)_4$	–40	Et_2O	77	64	*S*
21	**34**[d]	$Ti(OPi)_4$	–40	Et_2O	91	63	*S*

[a] 3 eq Et_2Zn; [b] 1.5 eq Et_2Zn; [c] 5% ligand used; [d] 20% ligand used;



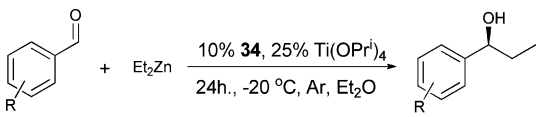
Scheme 8 Synthesis of ligands **33–37**.

We then examined a number of aromatic aldehydes. The electron-poor *ortho*-, *meta*- and *p*-chlorobenzaldehydes and the electron-rich methoxybenzaldehydes gave enantioselectivities ranging between 81 and 92% ee and moderate to good yields of alcohols, except 4-methoxybenzaldehyde; 1-naphthaldehyde gave only 17% yield and 60% ee. Methyl substituted benzaldehydes produced moderate yields of alcohols and very good enantioselection (88% and 89% ees). As can be seen from the Table 3, the best ee and yield of alcohol was accomplished using 2-methoxybenzaldehyde.

3. Conclusion

In summary, we have described in detail a synthetically valuable way of making sulfoximines and evaluation of their catalytic enantioselective effect in Et_2Zn addition to aldehydes in the absence and presence of $Ti(OPr^i)_4$. It is noteworthy that the preferred sulfoximine **34** was easily synthesised in five steps in an overall yield (41%) without the need for chromatography. In general, the best results are obtained with benzaldehyde and 2-methoxybenzaldehyde with enantioselectivities 90% ee and 92% ee respectively.

Table 3 Et_2Zn addition aromatic aldehydes **28**, **38–47** using ligand **34**



28, 38-47 **29, 48-57**

Aldehyde	ee[a] (%)	Yield[b] (%)	Configuration[c]
benzaldehyde **28**	90	67	*S*
2-chlorobenzaldehyde **38**	81	42	*S*
3-chlorobenzaldehyde **39**	89	54	—
4-chlorobenzaldehyde **40**	85	50	*S*
2-methoxybenzaldehyde **41**	92	73	*S*
3-methoxybenzaldehyde **42**	87	28	*S*
4-methoxybenzaldehyde **43**	58	5	*S*
3-methylbenzaldehyde **44**	89	55	*S*
4-methylbenzaldehyde **45**	88	63	*S*
1-naphthaldehyde **46**	60	17	*S*
2-pyridinecarboxaldehyde **47**	5	99	—

[a] Determined by GC using a β-dex (30 m × 0.25 mm × 0.25 μm) column. [b] Isolated yields. [c] Assigned by comparison of the chromatogram with those reported in the literature.[59–62]

4. Experimental

Melting points (°C) were obtained in an Electrothermal 9100 apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were performed on a Varian Mercury spectrometer at 400 and 100 MHz in $CDCl_3$ with tetramethylsilane as an internal standard and signals are evaluated using MestreC computer software. Elemental analysis was recorded on a LECO CHNS 932 elemental analyzer and IR spectra of all compounds were performed using Perkin Elmer spectrometer. Mass spectra were recorded on a Kratos Concept 1H Magnetic Sector Mass Spectrometer at Leicester University. Optical rotations of *enantio*–enriched compounds were recorded on a Labart WZZ-2A and Berlingham Bentley ADP220 at 589 nm using sodium D line wavelength light at room temperature with a path length of 10 cm. Concentrations are quoted in gdm^{-3} and values given have units of $g^{-1}L^{-1}\times10^{2}$. Enantiomeric excesses of alcohols were determined using a Hewlett-Packard 6850 gas chromatograph with a Supelco β-DEX™ column (30 m × 0.25 mm × 0.25 μm). Enantiomeric purity of ligands was determined by chiral HPLC (Hawlett Pachard 1200) analysis using a enantiopure stationary phase (Daicel Chiralcel OD-H), eluting with *i*-PrOH-hexane, and using UV detection at 254 nm. All crude products were examined by Thin Layer Chromatography (TLC) prior to purification. TLC was performed on silica gel 60 F_{254} on aluminium sheets with a 0.2 mm layer manufactured by Merck & Co and the visualising agent was UV fluorescence (254 nm). The Chromatotron (Harrison Research California) used for purification was model 7024T with circular Kieselgel 60 PF_{254} silica plates. Silica gel (230–400 mesh, supplied by Fluka) chromatographic purification was performed using silica packed glass columns (various sizes). The amount of silica used was approximately 40–60 times by weight relative to material applied to the column. The eluting solvents (hexane:ethyl acetate mixture in all cases), were reagent grade and used as received. Low temperature experiments (−70 °C) were carried out using HAAKE 90 cryostat for controlling the reaction bath temperature.

General procedure 1 for sulfoximination using 2-ethyl-3-aminoquinazolinone 1

3-Amino-2-ethyl-quinazolinone $Q^{1}NH_2$ **1** (0.3 g, 1.58 mmol) and acetic acid-free lead tetraacetate (LTA) (0.77 g, 1.75 mmol) were added alternately and continuously in very small portions over 15 min. to a vigorously stirred solution of dry dichloromethane (6 cm^3) at −40 °C. The mixture was then stirred for a further 5 min. to give a solution of the 3-acetoxyaminoquinazolinone. The temperature was lowered to −70 °C, before dropwise addition of dimethyl sulfoxide (0.25 g, 3.17 mmol) as a solution in dichloromethane (3 cm^3) containing HMDS (0.51 g, 3.17 mmol) and then the temperature of the solution allowed to rise to −10 °C (~1.5 to 2 h) with continuous stirring. Saturated aqueous sodium hydrogen carbonate (30 cm^3) was added and the mixture extracted with dichloromethane (3 × 30 cm^3). The organic layer was separated, washed with water (3 × 30 cm^3), dried with sodium sulfate and the solvent removed by evaporation under reduced pressure. The crude product crystallised on addition of ethanol to give sulfoximine **14** as a colourless solid (0.4 g, 95%) mp 130–132 °C (from ethanol) IR (in CH_2Cl_2 solution) ν_{max}/ cm^{-1}: 3479 w, 3011 w, 2929 w 1672 s, 1608 w, 1591 s and 1568 w. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.24 (3H, t, *J* 7.3 Hz, CH_2CH_3), 2.97 (2H, q, *J* 7.3 Hz, CH_2CH_3), 3.22 (6H, s, CH_3SCH_3), 7.25 to 7.59 (3H, m, 6-H, 7-H, 8-H (Q)) and 8.09 (1H, ddd, *J* 8.1 Hz and 2.2 and 1.4 Hz, 5-H (Q)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.8, 28.1, 42.7, 121.2, 126.1, 126.6, 127.2, 134.1, 146.7, 161.3 and 161.9). Elemental analysis calculated for $C_{12}H_{15}N_3O_2S$: C, 54.32, H, 5.70, N, 15.84, O, 12.06, S, 12.08%. Found: C, 54.35, H, 5.91, N, 15.95, S, 11.85%.

Sulfoximination of phenyl methyl sulfoxide using $Q^{1}NH_2$

General procedure 1 was followed using $Q^{1}NH_2$ **1** (0.3 g, 1.58 mmol), LTA (0.77 g, 1.75 mmol), HMDS (0.51 g, 3.17 mmol) and phenyl methyl sulfoxide **16a** (0.44 g, 3.17 mmol) in a solution in dichloromethane (6 cm^3). The crude product crystallised on addition of ethanol to give sulfoximine **17a** as a colourless solid (0.3 g, 57%) mp 145–147 °C (from ethanol) IR (in CH_2Cl_2 solution) ν_{max}/ cm^{-1}: 3586 w, 3064 w, 2974 w, 2934 w 1672 s, 1591 s and 1568 w. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.35 (3H, t, *J* 7.3 Hz, CH_2CH_3), 3.17 (2H, m, CH_2CH_3), 3.31 (3H, s, $PhSCH_3$), 7.39 to 7.75 (6H, m, 6-H, 7-H, 8-H (Q) and 3H (Ph)), 8.21 (1H, dd, *J* 8.2 Hz and 1.1 Hz, 5-H (Q)) and 8.33 (2H, dd, 8.4 Hz and 1.7 Hz, 2H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.8, 28.2, 43.8, 121.3, 126.2, 127.3, 128.8, 129.6, 134.1, 137.3, 146.8, 161.5 and 161.8). Elemental analysis calculated for $C_{17}H_{17}N_3O_2S$: C, 62.36, H, 5.23, N, 12.83, O, 9.77, S, 9.79%. Found: C, 62.13, H, 5.35, N, 12.97, S, 9.87%.

Sulfoximination of phenyl ethyl sulfoxide using $Q^{1}NH_2$

General procedure 1 was followed using $Q^{1}NH_2$ **1** (0.2 g, 1.1 mmol), LTA (0.52 g, 1.16 mmol), HMDS (0.34 g, 2.12 mmol) and phenyl ethyl sulfoxide **16b** (0.33 g, 2.12 mmol) in a solution in dichloromethane (6 cm^3). The crude product crystallised on addition of ethanol to give sulfoximine **17b** as a colourless solid (0.22 g, 61%) mp 155–157 °C (from ethanol) IR (in CH_2Cl_2 solution) ν_{max}/ cm^{-1}: 3494 w, 3065 w, 2978 w, 2937 w, 2875 w 1675 s, 1592 w and 1568 w. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.21 (3H, t, *J* 7.6 Hz, SCH_2CH_3), 1.34 (3H, t, *J* 7.3 Hz, QCH_2CH_3), 3.2 (2H, m, QCH_2CH_3), 3.51 (3H, m, SCH_2CH_3), 7.25 to 7.72 (6H, m, 6-H, 7-H, 8-H (Q) and 3H (Ph)), 8.17 (1H, ddd, *J* 8.4, 2.2 and 0.7 Hz, 5-H (Q)) and 8.24 (2H, ddd, 8.4, 6.9 and 1.4 Hz, 2H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 8.2, 10.9, 28.3, 50.1, 121.2, 126.1, 126.8, 127.2, 129.4, 129.5, 134.0, 134.2, 135.5, 146.8, 161.5 and 162.0). Elemental analysis calculated for $C_{18}H_{19}N_3O_2S$: C, 63.32, H, 5.61, N, 12.31, O, 9.37, S, 9.39%. Found: C, 63.37, H, 5.68, N, 12.43, S, 9.36%.

Sulfoximination of phenyl isopropyl sulfoxide using $Q^{1}NH_2$

General procedure 1 was followed using $Q^{1}NH_2$ **1** (0.2 g, 1.1 mmol), LTA (0.52 g, 1.16 mmol), HMDS (0.34 g, 2.12 mmol) and phenyl isopropyl sulfoxide **16c** (0.36 g, 2.12 mmol) in a solution in dichloromethane (6 cm^3). The crude product crystallised on addition of ethanol to give sulfoximine **17c** as a colourless solid (0.23 g, 61%) mp 119–121 °C (from ethanol) IR (in CH_2Cl_2 solution) ν_{max}/ cm^{-1}: 3064 w, 2978 w, 2936 w, 2873 w, 1678 s, 1591 s and 1568 w. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.22 (3H, d, *J* 6.9 Hz, CH_3CHCH_3), 1.35 (3H, t, *J* 7.3 Hz, QCH_2CH_3), 1.48 (3H, d, *J* 6.9 Hz, CH_3CHCH_3), 3.16 (2H, m, QCH_2CH_3), 3.87 (1H, m, CH_3CHCH_3), 7.27 to 7.76 (6H, m, 6-H, 7-H, 8-H (Q) and 3H

(Ph)), 8.25 (3H, m, 5-H (Q)) and 2H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.0, 16.1, 17.3, 28.6, 29.3, 57.5, 121.2, 125.9, 126.7, 127.0, 129.4, 129.1, 129.7, 133.7, 133.8, 146.6, 161.4 and 161.5). Elemental analysis calculated for $C_{19}H_{21}N_3O_2S$: C, 64.20, H, 5.95, N, 11.82, O, 9.00, S, 9.02%. Found: C, 64.24, H, 6.09, N, 11.92, S, 8.82%.

Sulfoximination of phenyl *tert*-butyl sulfoxide using Q^1NH_2

General procedure 1 was followed using Q^1NH_2 **1** (0.15 g, 0.8 mmol), LTA (0.38 g, 0.87 mmol), HMDS (0.25 g, 1.58 mmol) and phenyl *tert*-butyl sulfoxide **16d** (0.25 g, 1.38 mmol) in a solution in dichloromethane (6 cm^3). The crude product crystallised on addition of ethanol to give sulfoximine **17d** as a colourless solid (0.18 g, 60%) mp 127–128 °C (from ethanol) IR (in CH_2Cl_2 solution) $\nu_{max/}$ cm^{-1}: 3065 w, 2977 w, 2934 w 1679 s, 1591 s and 1568 w. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.38 (3H, t, *J* 7.3 Hz, QCH_2CH_3), 1.53 (9H, s, ^{t}Bu), 3.10–3.36 (2H, m, QCH_2CH_3), 7.24 to 7.69 (6H, m, 6-H, 7-H, 8-H (Q) and 3H (Ph)), 8.03 (1H, dd, *J* 7.69 and 1.1 Hz, 5-H (Q)) and 8.10 (2H, dd, 8.7, and 1.4 Hz, 2H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.2, 24.6, 28.8, 63.7, 121.3, 125.7, 126.7, 126.8, 128.6, 131.4, 133.6, 134.9, 135.1, 146.4, 161.2 and 161.5). Elemental analysis calculated for $C_{20}H_{23}N_3O_2S$: C, 65.01, H, 6.27, N, 11.37, O, 8.66, S, 8.68%. Found: C, 65.04, H, 6.22, N, 11.50, S, 8.51%.

Sulfoximination of phenyl benzyl sulfoxide using Q^1NH_2

General procedure 1 was followed using Q^1NH_2 **1** (0.2 g, 1.1 mmol), LTA (0.52 g, 1.16 mmol), HMDS (0.34 g, 2.12 mmol) and phenyl benzyl sulfoxide **16e** (0.46 g, 2.12 mmol) in a solution in dichloromethane (6 cm^3). The crude product crystallised on addition of ethanol to give sulfoximine **17e** as a colourless solid (0.25 g, 62%) mp 136–138 °C (from ethanol) IR (in CH_2Cl_2 solution) $\nu_{max/}$ cm^{-1}: 3064 w, 2936 w, 2858 w, 1678 s, 1608 w, 1591 s and 1568 w. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.31 (3H, t, *J* 7.3 Hz, QCH_2CH_3), 3.11 (2H, m, QCH_2CH_3), 4.71 (2H, s, $PhCH_2$), 6.93 (2H, dd, J 6.9 and 1.4 Hz, 2H (Ph)), 7.12 to 7.72 (9H, m, 6-H, 7-H, 8-H (Q) and 6H (Ph)), 7.99 (2H, ddd, 8.4, 2.9 and 1.8 Hz, 2H (Ph)) and 8.22 (1H, ddd, *J* 8.4, 7.3 and 0.7 Hz, 5-H (Q)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.9, 28.2, 62.6, 121.3, 126.2, 126.8, 127.3, 128.0, 128.6, 129.0, 129.2, 129.6, 131.2, 134.1, 134.2, 135.0, 146.8, 161.6 and 162.2). Elemental analysis calculated for $C_{23}H_{21}N_3O_2S$: C, 68.46, H, 5.25, N, 10.41, O, 7.93, S, 7.95%. Found: C, 68.26, H, 5.28, N, 10.50, S, 7.94%.

Sulfoximination of phenyl c-hexyl sulfoxide using Q^1NH_2

General procedure 1 was followed using Q^1NH_2 **1** (0.2 g, 1.1 mmol), LTA (0.52 g, 1.16 mmol), HMDS (0.34 g, 2.12 mmol) and phenyl c-hexyl sulfoxide **16f** (0.44 g, 2.12 mmol) in a solution in dichloromethane (6 cm^3). The crude product crystallised on addition of ethanol to give sulfoximine **17f** as a colourless solid (0.29 g, 70%) mp 161–163 °C (from ethanol) IR (in CH_2Cl_2 solution) $\nu_{max/}$ cm^{-1}: 3480 w, 3064 w, 3031 w, 2981 w, 2936 w, 2874 w, 1672 s, 1608 w, 1592 s and 1568 w. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.07–1.91 (9H, m, 9H(c-Hex)),1.35 (3H, t, *J* 7.3 Hz, QCH_2CH_3), 2.42 (1H, dd, *J* 12.4 and 6.9 Hz, 1H (c-Hex)), 3.17 (2H, m, QCH_2CH_3), 3.59 (1H, m, SC*H*), 7.28–7.65 (6H, m, 6-H, 7-H, 8-H (Q) and 3H (Ph)), 8.08 (3H, m, 2H (Ph)) and 5-H (Q)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.1, 25.2, 25.52, 25.56, 25.89, 26.6, 28.6, 64.7, 121.3, 125.8, 126.8, 126.9, 129.0, 129.8, 133.6, 133.7, 136.1, 146.6, 161.5 and 162.6). Elemental analysis calculated for $C_{22}H_{25}N_3O_2S$: C, 66.81, H, 6.37, N, 10.62, O, 8.09, S, 8.11%. Found: C, 66.46, H, 6.45, N, 10.78, S, 8.18%.

Sulfoximination of dimethyl sulfoxide using Q^2NH_2

General procedure 1 was followed using Q^2NH_2 **18** (0.3 g, 1.46 mmol), LTA (0.71 g, 1.61 mmol), HMDS (0.34 g, 2.12 mmol) and DMSO **16h** (0.23 g, 2.93 mmol) in a solution in dichloromethane (5 cm^3). The crude product was then chromatographed over silica and eluting with hexane–ethyl acetate 1 : 1 gave sulfoximine **27** (R_f 0.23) as a colourless oil (0.26 g, 64%). $[\alpha]_D$ = +46.7 (*c* = 0.87, $CHCl_3$), (Found: MH$^+$ 282.0908. $C_{12}H_{17}N_3O_3S$ requires *M* 282.0912), IR (in CH_2Cl_2 solution) $\nu_{max/}$ cm^{-1}: 3450 m, 3055 w, 2960 w, 2895 m, 2840 w, 1684 s, 1605 s and 1572 w. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.57 (3H, d, *J* 6.4 Hz, $CHOHCH_3$), 3.34 (3H, s, CH_3SCH_3), 3.35 (3H, s, CH_3SCH_3), 4.36 (1H, d, *J* 6.4 Hz, $CHOHCH_3$), 5.27 (1H, m, $CHOHCH_3$), 7.47 (1H, t, *J* 7.3, 7-H, (Q)), 7.70–7.77 (2H, m, 6-H, 8-H (Q)) and 8.24 (1H, dd, *J* 1.1 Hz and 8.06 Hz, 5-H (Q)). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 17.7, 21.5, 42.2, 42.6, 44.0, 44.2, 65.6, 68.1, 121.4, 121.8, 126.7, 126.8, 126.9, 127.1, 127.3, 127.9, 134.2, 134.4, 145.9, 146.3, 156.7, 161.1, 161.9, 170.8,

Sulfoximination of phenyl methyl sulfoxide using Q^2NH_2

General procedure 1 was followed using Q^2NH_2 **18** (0.2 g, 0.97 mmol), LTA (0.47 g, 1.07 mmol), HMDS (0.31 g, 1.94 mmol) and phenyl methyl sulfoxide **16a** (0.27 g, 1.95 mmol) in a solution in dichloromethane (6 cm^3) to give sulfoximine **20** as a colorless oil. The crude product contained a 1.3 : 1 ratio of sulfoximine diastereoisomers from comparison of signals at δ 3.36 and 3.32 in its NMR spectrum (see below). The crude product was then chromatographed over silica and eluting with hexane–ethyl acetate 2 : 1 gave minor sulfoximine **20a** diastereoisomer (R_f 0.2) as a colourless oil (0.1 g, 29%).

$[\alpha]_D$ −49.2 (*c* 0.5, $CHCl_3$) (Found: MH$^+$ 344.1069. $C_{17}H_{18}N_3O_3S$ requires *M* 344.1069), IR (in CH_2Cl_2 solution) $\nu_{max/}$ cm^{-1}: 3440 m, 3066 w, 2963 w, 2926 m, 2855 w, 1671 s, 1595 s and 1569 w. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.57 (3H, d, *J* 6.6 Hz, $CHOHCH_3$), 3.36 (3H, s, $PhSCH_3$), 5.37 (1H, q, J 6.6 Hz, $CHOHCH_3$) 7.39 to 7.75 (6H, m, 6-H, 7-H, 8-H (Q) and 3H (Ph)), 8.16 (1H, ddd, *J* 8.7 Hz, 1.4 Hz and 0.7 Hz, 5-H (Q)) and 8.33 (2H, dd, 8.4 Hz and 1.5 Hz, 2H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.9, 44.9, 66.1, 121.4, 126.8, 126.9, 127.4, 128.2, 129.6, 129.8, 134.3, 138.4, 145.9, 160.5 and 161.4).

Further elution with the same solvent mixture gave major sulfoximine **20b** diastereoisomer (R_f 0.12) as an oil (0.13 g, 37%). $[\alpha]_D$ −34.2 (*c* 0.5, $CHCl_3$) (Found: MH$^+$ 344.1068. $C_{17}H_{18}N_3O_3S$ requires *M* 344.1069), IR (in CH_2Cl_2 solution) $\nu_{max/}$ cm^{-1}: 3456 w, 2964 m, 2928 m, 1739 s, 1671 s, 1597 s and 1569 w. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.52 (3H, d, *J* 6.6 Hz, $CHOHCH_3$), 3.32 (3H, s, $PhSCH_3$), 5.38 (1H, q, J 6.6 Hz, $CHOHCH_3$) 7.43 to 7.76 (6H, m, 6-H, 7-H, 8-H (Q) and 3H (Ph)), 8.24 (1H, dd, *J* 8.1 Hz and 1.1 Hz, 5-H (Q)) and 8.33 (2H, dd, 8.8 Hz and 1.5 Hz, 2H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.8, 44.3, 65.6, 121.5,

126.8, 127.1, 127.3, 128.4, 129.8, 134.4, 134.5, 137.3, 145.9, 161.7 and 161.8).

Sulfoximination of phenyl ethyl sulfoxide using Q^2NH_2

General procedure 1 was followed using Q^2NH_2 **18** (2.2 g, 11.7 mmol), LTA (6.21 g, 14.03 mmol), HMDS (3.77 g, 23.37 mmol) and phenyl ethyl sulfoxide **16b** (3.6 g, 23.37 mmol) in a solution in dichloromethane (20 cm^3) to give sulfoximine **21** as a colourless oil. The crude product contained a 1 : 1 ratio of sulfoximine diastereoisomers from comparison of signals at δ 1.53 and 1.60 in its NMR spectrum (see below). The crude product was then chromatographed over silica and eluting with hexane–ethyl acetate 2 : 1 gave one sulfoximine diastereoisomer **21a** (R_f 0.2) as a colourless oil (1.59 g, 38%). $[\alpha]_D$ −33.5 (*c* 0.67, $CHCl_3$) (Found: MH^+ 358.1224. $C_{18}H_{20}N_3O_3S$ requires *M* 358.1225), IR (in CH_2Cl_2 solution) $\nu_{max/}$ cm^{-1}: 3436 m, 3065 w, 2978 m, 2933 m, 1675 s, 1595 s and 1569 w. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.19 (3H, t, *J* 7.3 Hz, CH_2CH_3), 1.53 (3H, d, *J* 6.6 Hz, $CHOHCH_3$), 3.51 (2H, m, CH_2CH_3), 5.39 (1H, q, J 6.6 Hz, $CHOHCH_3$) 7.41 to 7.74 (6H, m, 6-H, 7-H, 8-H (Q) and 3H (Ph)), 8.18 to 8.23 (3H, m, 5-H (Q)) and 2H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 8.3, 21.8, 50.7, 65.6, 121.3, 126.8, 127.0, 127.2, 129.0, 129.6, 134.3, 134.4, 135.3, 145.8, 161.5 and 161.9). Further elution with the same solvent mixture gave other sulfoximine diastereoisomer **21b** (R_f 0.1) as an oil (1.56 g, 37%). $[\alpha]_D$ −57.4 (*c* 0.42, $CHCl_3$) (Found: MH^+ 358.1225. $C_{18}H_{20}N_3O_3S$ requires *M* 358.1225), ^1H NMR ($CDCl_3$, 400 MHz): δ 1.31 (3H, t, *J* 7.3 Hz, CH_2CH_3), 1.60 (3H, d, *J* 6.6 Hz, $CHOHCH_3$), 3.57 (2H, m, CH_2CH_3), 4.45 (1H, b, $CHOHCH_3$), 5.41 (1H, b, $CHOHCH_3$) 7.35 to 7.69 (6H, m, 6-H, 7-H, 8-H (Q) and 3H (Ph)), 8.11 (3H, d, 6.9 Hz, 5-H (Q)) and 2H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 7.6, 21.2, 51.0, 65.9, 121.4, 126.7, 126.9, 127.2, 128.8, 129.4, 134.0, 134.2, 137.2, 145.8, 160.8 and 161.4).

Sulfoximination of phenyl isopropyl sulfoxide using Q^2NH_2

General procedure 1 was followed using Q^2NH_2 **18** (0.5 g, 2.44 mmol), LTA (1.19 g, 2.68 mmol), HMDS (0.79 g, 4.88 mmol) and phenyl isopropyl sulfoxide **16c** (0.82 g, 4.88 mmol) in a solution in dichloromethane (10 cm^3) to give sulfoximine **22**. The crude product contained a 1 : 1 ratio of sulfoximine diastereoisomers from comparison of signals at δ 5.41 and 5.29 in its NMR spectrum (see below). The crude product was then recrystallised on addition of ethanol gave 1.4 : 1 diastereoisomeric mixture of sulfoximine **22** as a colourless solid (0.61 g, 71%) mp 84–87 °C (from ethanol). IR (in $CHCl_3$ solution) $\nu_{max/}$ cm^{-1}: 3431 w, 3065 w, 2980 w, 2934 w, 1675 s, 1594 s and1569m. ^1H NMR ($CDCl_3$, 400 MHz): signals belong to mixture of diastereoisomers observable at δ 1.09–1.69 (18H, aliphatic protons), 3.82 (4H, m, *J* 6.96 Hz, $CH(CH_3)_2$), 4.41 (2H, b, $CHOHCH_3$), 4.51 (2H, b, $CHOHCH_3$), 5.29 (1H, m, *J* 6.6 Hz, $CHOHCH_3$), 5.41 (1H, m, *J* 6.6 Hz, $CHOHCH_3$), 7.29–8.14 (9H, m, 5-H, 6-H, 7-H, 8-H (Q) and 5H (Ph). Elemental analysis calculated for $C_{19}H_{21}N_3O_3S$: C, 61.44; H, 5.70; N, 11.31;S, 8.63%. Found: C, 60.96, H, 5.70, N, 11.23, S, 8.41%.

Sulfoximination of phenyl *tert*-butyl sulfoxide using Q^2NH_2

General procedure 1 was followed using Q^2NH_2 **18** (0.6 g, 2.93 mmol), LTA (1.56 g, 2.93 mmol), HMDS (0.94 g, 5.85 mmol) and phenyl *t*-butyl sulfoxide **16d** (1.06 g, 5.85 mmol) in a solution in dichloromethane (10 cm^3) to give sulfoximine **23** as a colourless solid. The crude product contained a 1 : 1 ratio of sulfoximine diastereoisomers from comparison of signals at δ 5.44 and 5.53 in its NMR spectrum (see below). The crude product was then chromatographed using chromatotron chromatography eluting with hexane–ethyl acetate 2 : 1 gave one sulfoximine diastereoisomer **23a** (R_f 0.3). The product crystallised on addition of ethanol to give as a colourless solid (0.83 g, 34%) mp 156–157 °C (from ethanol). $[\alpha]_D$ = +61.347 (*c* = 0.47, $CHCl_3$) IR (in CH_2Cl_2 solution) $\nu_{max/}$ cm^{-1}: 3431 w, 3066 w, 2957 m, 2925 s, 2870 m, 2851 m, 1680 s, 1594 s and1570m. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.52 (9H, s, $C(CH_3)_3$), 1.61 (3H, d, *J* 6.23 Hz, $CHOHCH_3$), 4.57 (1H, d, *J* 6.96 Hz, $CHOHCH_3$), 5.53 (1H, m, $CHOHCH_3$), 7.28–7.65 (6H, m, 6-H, 7-H, 8-H (Q) and 3H (Ph)) and 8.01–8.12 (3H, m, 5-H (Q)) and 2H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.1, 24.5, 63.5, 65.5, 121.5, 126.4, 126.7, 127.0., 128.6, 131.5, 133.7, 133.9, 135.3, 145.4, 161.1 and 161.8. Elemental analysis calculated for $C_{20}H_{23}N_3O_3S$: C, 62.32; H, 6.01; N, 10.90; S, 8.32%. Found: C, 62.95; H, 6.09; N, 11.07, S, 8.36%.

Further elution with the same solvent mixture gave other *sulfoximine* diastereoisomer **23b** (R_f 0.17). The product crystallised on addition of ethanol to give as a colourless solid (0.83 g, 34%) mp 151–153 °C (from ethanol) $[\alpha]_D$ = +67.476 (*c* = 0.48, $CHCl_3$) IR (in $CHCl_3$ solution) $\nu_{max/}$ cm^{-1}: 3444 w, 3066 w, 2956 m, 2925 s, 2870 m, 2851 m, 1671 s, 1595 s and1569 w. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.51 (9H, s, $C(CH_3)_3$), 1.64 (3H, d, *J* 6.6 Hz, $CHOHCH_3$), 4.44 (1H, d, *J* 6.9 Hz $CHOHCH_3$), 5.44 (1H, m, *J* 6.6 Hz, $CHOHCH_3$), 7.30–7.66 (6H, m, 6-H, 7-H, 8-H (Q), 3H (Ph)), 7.90 (2H, d, *J* 7.3 Hz, 2H (Ph)) and 8.04 (1H, d, *J* 8.1 Hz, 5-H (Q)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.1, 24.8, 64.7, 65.9, 121.1, 126.5, 126.9, 127.1, 127.0, 130.0, 133.4, 133.9, 135.6, 145.5, 159.8 and 160.3. Elemental analysis calculated for $C_{20}H_{23}N_3O_3S$: C, 62.32; H, 6.01; N, 10.90; S, 8.32%. Found: C, 62.86, H, 5.86, N, 11.12, S, 8.38%.

Sulfoximination of phenyl c-hexyl sulfoxide using Q^2NH_2

General procedure 1 was followed using Q^2NH_2 **18** (0.5 g, 2.44 mmol), LTA (1.19 g, 2.68 mmol), HMDS (0.79 g, 4.88 mmol) and phenyl c-hexyl sulfoxide **16f** (1.02 g, 4.88 mmol) in a solution in dichloromethane (10 cm^3) to give sulfoximine **25**. The crude product contained a 1 : 1 ratio of sulfoximine diastereoisomers from comparison of signals at δ 5.34 and 5.45 in its NMR spectrum. Attempted chromatographic separation was unsuccessful. The crude product was then recrystallised on addition of ethanol to give a 95% diastereoisomeric excess of sulfoximine **25a** as a colourless solid (0.7 g, 70%) mp 169–170 °C (from ethanol). $[\alpha]_D$ = +71.25 (*c* = 0.4, $CHCl_3$). IR (in $CHCl_3$ solution) $\nu_{max/}$ cm^{-1}: 3431 w, 3065 w, 2926 s, 2855 s, 1670 s, 1594 s and1569m. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.11–1.98 (10H, m, $(CH_2)_5CHS$), 1.59 (3H, d, *J* 6.2 Hz, $CHOHCH_3$), 3.53 (1H, t, *J* 12.1 Hz, $(CH_2)_5CHS$), 4.51 (1H, d, *J* 6.9 Hz, $CHOHCH_3$), 5.45 (1H, p, *J* 6.2 Hz, $CHOHCH_3$) and 7.29–8.03 (9H, m, 5-H, 6-H, 7-H, 8-H (Q) and 5H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.9, 25.2, 25.4, 25.5, 25.7, 25.9, 63.9, 65.6, 121.5, 126.4, 126.92, 126.97, 129.0, 129.8, 133.7, 134.0, 136.7, 145.6, 161.1 and 161.7. Elemental analysis calculated for $C_{22}H_{25}N_3O_3S$: C, 64.21; H, 6.12; N, 10.21; S, 7.79%. Found: C, 64.71, H, 6.06, N, 10.30, S, 7.86%.

Sulfoximination of phenyl benzyl sulfoxide using Q^2NH_2

General procedure 1 was followed using Q^2NH_2 **18** (0.6 g, 2.93 mmol), LTA (1.56 g, 3.51 mmol), HMDS (0.94 g, 5.85 mmol) and phenyl benzyl sulfoxide **16e** (1.26 g, 5.85 mmol) in a solution in dichloromethane (10 cm^3) to give sulfoximine **24**. The crude product contained a 1 : 1 ratio of sulfoximine diastereoisomers from comparison of signals at δ 5.35 and 5.12 in its NMR spectrum (see below). The crude product was then chromatographed using a chromatotron and eluting with hexane–ethyl acetate 2 : 1 gave one sulfoximine diastereoisomer **24a** (R_f 0.27). The product crystallised on addition of ethanol to give a colourless solid (0.39 g, 32%) mp 146–148 °C (from ethanol). $[\alpha]_D$ = +36.773 (c = 0.55, $CHCl_3$) IR (in CH_2Cl_2 solution) $\nu_{max/}$ cm^{-1}: 3446 w, 3032 w, 3065 w, 2927 w, 1675 s, 1595 s and 1569m. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.48 (3H, d, J 6.2 Hz, CHOHCH_3), 4.37 (1H, d, J 5.9 Hz, CHOHCH$_3$), 4.71 (2H, s, SCH_2Ph), 5.35 (1H, m, CHOHCH$_3$), 7.13–7.95 (11H, m, 6-H, 7-H, 8-H (Q), 5H (Ph) and 3H(Bn)) and 8.27 (1H, d, J 8.1 Hz, 5-H (Q)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.8, 63.3, 65.7, 121.4, 126.9, 127.1, 127.3, 127.9, 128.7, 129.1, 129.2, 129.3, 131.3, 134.3, 134.4, 135.1, 145.9, 161.6 and 162.1. Elemental analysis calculated for $C_{23}H_{21}N_3O_3S$: C, 65.85; H, 5.05; N, 10.02; S, 7.64%. Found: C, 66.58; H, 5.11; N, 10.20, S, 7.88%.

Further elution with the same solvent mixture gave the other *sulfoximine* diastereoisomer **24b** (R_f 0.15). The product crystallised on addition of ethanol to give as a colourless solid (0.39 g, 32%) mp 201–203 °C (from ethanol). $[\alpha]_D$ = +48.505 (c = 0.54, $CHCl_3$) IR (in $CHCl_3$ solution) $\nu_{max/}$ cm^{-1}: 3440 w, 3065 w, 3033 w, 2958 w, 2927 w, 2870 w, 2246 w, 1670 s, 1595 s and 1569m. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.49 (3H, d, J 6.2 Hz, CHOHCH_3), 4.31 (1H, d, J 5.9 Hz, CHOHCH$_3$), 4.74 (1H, d, J 13.9 SCHHPh), 4.79 (1H, d, J 13.9 SCHHPh), 5.12 (1H, m, CHOHCH$_3$), 7.10 (1H, d, J 7.3 Hz, 2H(Bn)), 7.22–7.94 (11H, m, 6-H, 7-H, 8-H (Q), 5H (Ph) and 3H(Bn)) and 8.17 (1H, d, J 8.06 Hz, 5-H (Q)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.4, 63.7, 65.8, 121.4, 126.7, 127.0, 127.3, 127.4, 128.6, 128.8, 128.9, 129.2, 129.4, 131.5, 133.9, 134.2, 137.4, 145.9, 160.8 and 161.6. Elemental analysis calculated for $C_{23}H_{21}N_3O_3S$: C, 65.85; H, 5.05; N, 10.02; S, 7.64%. Found: C, 66.29, H, 5.01, N, 10.10, S, 7.80%.

Sulfoximination of diphenyl sulfoxide using Q^2NH_2

General procedure 1 was followed using Q^2NH_2 **18** (2 g, 9.75 mmol), LTA (5.19 g, 11.71 mmol), HMDS (3.15 g, 19.5 mmol) and diphenyl sulfoxide **16g** (2.37 g, 11.71 mmol) in a solution in dichloromethane (25 cm^3) to give sulfoximine **26**. The crude product was then crystallised on addition of ethanol gave sulfoximine **26** as a colourless solid (3 g, 76%) mp 136–38 °C (from ethanol). $[\alpha]_D$ = +36.399 (c = 0.53, $CHCl_3$), IR (in $CHCl_3$ solution) $\nu_{max/}$ cm^{-1}: 3438 w, 3065 w, 2956 w, 2928 w, 2247 w, 1670 s, 1595 s and 1569m. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.61 (3H, d, J 6.6 Hz, CHOHCH_3), 4.43 (1H, d, J 6.2 Hz, CHOHCH$_3$), 5.51 (1H, t, J 6.2 CHOHCH$_3$), 7.32–7.67 (9H, m, 6-H, 7-H, 8-H (Q) and 6H (Ph)), 8.01–8.08 (3H, m, 5-H (Q)) and 2H (Ph) and 8.27 (2H, dd, J 8.8 and 1.5 Hz, 2H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.9, 65.9, 121.4, 126.6, 127.0, 128.6, 128.8, 129.2, 129.6, 133.5, 133.9, 134.1, 139.2, 139.3, 145.5, 160.7 and 161.1. Elemental analysis calculated for $C_{22}H_{19}N_3O_3S$: C, 65.17; H, 4.72; N, 10.36; S, 7.91%. Found: C, 65.74, H, 4.80, N, 10.44, S, 7.93%.

Sulfoximination of diphenyl sulfoxide using Q^4NH_2

General procedure 1 was followed using Q^4NH_2 **31** (2.1 g, 6.437 mmol), LTA (2.184 g, 7.725 mmol), HMDS (2.08 g, 19.5 mmol) and diphenyl sulfoxide **16g** (2.36 g, 7.724 mmol) in a solution in dichloromethane (25 cm^3) to give sulfoximine **34**. The crude product was then crystallised on addition of ethanol gave sulfoximine **34** as a colourless solid (1.98 g, 71%) mp 164–166 °C (from ethanol). $[\alpha]_D$ = +45.1 (c = 1.1, $CHCl_3$), IR (in $CHCl_3$ solution) $\nu_{max/}$ cm^{-1}: 3430 w, 3064 w, 2961 w, 2929 w, 2870 w, 1681 s, 1529 s and 1569m. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.72 (3H, d, J 6.9 Hz, CH_3CH$_3$CH), 1.07 (3H,d, J 6.9 Hz, CH$_3$CH_3CH), 2.65 (1H, m, CH$_3$CH$_3$CH), 4.17 (1H, b, CHCHOH), 5.28 (1H, b, CHCHOH) and 7.71 (14H m., 5-H, 6-H, 7-H, 8-H (Q), 10H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.8, 20.4, 30.7, 121.19, 126.5, 126.9, 128.4, 128.6, 129.1, 129.5, 133.2, 133.7, 133.9, 139.91, 139.93, 145.2, 159.6 and 160.7. Elemental analysis calculated for $C_{24}H_{23}N_3O_3S$: C, 66.49; H, 5.35; N, 9.69; S, 7.40%. Found: C, 66.41; H, 5.31; N, 9.66, S, 7.43%.

Sulfoximination of diphenyl sulfoxide using Q^3NH_2

General procedure 1 was followed using Q^3NH_2 **30** (300 mg, 1.215 mmol), LTA (656 mg, 1.458 mmol), HMDS (392 mg, 2.43 mmol) and diphenyl sulfoxide **16g** (368 mg, 1.822 mmol) in a solution in dichloromethane (6 cm^3) to give sulfoximine **33**. The crude product was then chromatographed using column chromatography eluting with hexane–ethyl acetate 3 : 1 gave sulfoximine **33** as a light yellow solid (412 mg, 71%) mp 66–67 °C (from ethanol). $[\alpha]_D$ = +64.0 (c = 1.5, $CHCl_3$), IR (in $CHCl_3$ solution) $\nu_{max/}$ cm^{-1}: 3485 w, 3064 w, 2953 w, 2953 w, 2867 w, 1678 s, 1608 w, 1588 s and 1567m. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.04 (9 H, s, (CH_3)$_3$C), 3.66 (1 H, d, J 9.7 Hz, CCHOH), 5.46 (1 H, d, J 9.7 Hz, CCHOH) and 7.20–8.34 (14 H, m, 5-H, 6-H, 7-H, 8-H (Q), 10H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 26.3, 38.0, 74.9, 121.3, 126.5, 126.8, 127.1, 128.5, 128.9, 129.0, 129.6, 133.1, 133.7, 133.8, 139.4, 139.6, 145.3, 159.9 and 160.4.

Sulfoximination of diphenyl sulfoxide using Q^5NH_2

General procedure 1 was followed using Q^5NH_2 **32** (500 mg, 2.146 mmol), LTA (995 mg, 2.25 mmol), HMDS (604 mg, 3.744 mmol) and diphenyl sulfoxide **16g** (567 mg, 2.81 mmol) in a solution in dichloromethane (10 cm^3) to give sulfoximine **35**. The crude product was then crystallised on addition of ethanol gave sulfoximine **35** as a colourless solid (670 mg, 77%) mp 178–180 °C (from ethanol). $[\alpha]_D$ = +5.0 (c = 0.8, $CHCl_3$), IR (in $CHCl_3$ solution) $\nu_{max/}$ cm^{-1}: 3385 w, 3063 w, 2924 w, 1681 s, 1593 s and 1568m. (Found: MH^+ 468.1374. $C_{27}H_{22}N_3O_3S$ requires M 468.1382), ^1H NMR ($CDCl_3$, 400 MHz): δ 5.21 (1H, d, J 6.2 Hz, PhCHOH), 6.29 (1H, d, J 6.2 Hz, PhCHOH) and 7.60 (19H, m. 5-H, 6-H, 7-H, 8-H (Q), 15H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 71.7, 121.3, 126.7, 127.1, 127.9, 128.1, 128.14, 128.2, 128.5, 129.1, 129.4, 133.0, 133.3, 134.1, 140.4, 140.6, 140.8, 145.3, 158.4 and 160.4.

Sulfoximination of phenyl isopropyl sulfoxide using Q^4NH_2

General procedure 1 was followed using Q^4NH_2 **31** (500 mg, 2.146 mmol), LTA (1.14 g, 2.575 mmol), HMDS (693 mg,

4.292 mmol) and phenyl *tert*-butyl sulfoxide **16d** (586 mg, 3.218 mmol) in a solution in dichloromethane (10 cm^3) to give sulfoximine **37**. The crude product contained a 1 : 1 ratio of sulfoximine diastereoisomers from comparison of signals at δ 5.16 and 5.37 ppm in its NMR spectrum (see below). The crude product was then chromatographed using column chromatography eluting with hexane–ethyl acetate 4 : 1 gave one sulfoximine diastereoisomer **37a** (R_f 0.28). The product crystallised on addition of ethanol to give sulfoximine **37a** as a colourless solid (298 mg, 34%) mp 141–143 °C (Decomposed) (from ethanol). $[\alpha]_D$ = +65.0 (c = 0.55, $CHCl_3$), IR (in $CHCl_3$ solution) $\nu_{max/}$ cm^{-1}: 3419 w, 3065 w, 2962 w, 2930 w, 2871 w, 1686 s, 1608 w, 1591 s and 1570m. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.69 (3H, d, J 6.9 Hz, CH_3CH$_3$CHCH), 1.19 (3H, d, J 6.9 Hz, CH$_3$CH_3CHCH), 1.53 (9H, s, (CH_3)$_3$C)), 2.68 (1H, dtd, J 13.7, 7.0, 6.9, 2.6 Hz, CH$_3$CH$_3$CHCH), 4.31 (1H, b, CHCHOH), 5.38 (1H, b, CHCHOH) and 7.27–8.18 (9H, m, 5-H, 6-H, 7-H, 8-H (Q), 5H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.8, 20.4, 24.5, 30.6, 63.4, 72.7, 121.4, 126.3, 126.8, 126.9, 128.6, 131.5, 133.6, 133.8, 135.4, 145.0, 160.3 and 161.1. Elemental analysis calculated for $C_{22}H_{27}N_3O_3S$: 63.90; H, 6.58; N, 10.16; S, 7.75%. Found: C, 63.60; H, 6.41; N, 10.18, S, 7.47%.

Further elution with the same solvent mixture gave sulfoximine **37b** diastereoisomer (R_f 0.2) as a colourless solid (298 mg, 34%). mp 152–153 °C (Decomposed) (from ethanol). $[\alpha]_D$ = +233.6 (c = 0.47, $CHCl_3$) IR (in CH_2Cl_2 solution) $\nu_{max/}$ cm^{-1}: 3430 w, 3065 w, 2964 w, 2930 w, 2871 w, 1681 s, 1592 s and 1569m. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.74 (3H, d, J 6.8 Hz, CH_3CH$_3$CHCH), 1.14 (3H, d, J 6.8 Hz, CH$_3$CH_3CHCH), 1.51 (9H, s, (CH_3)$_3$C)), 2.64 (1H, dtd, J 14.0, 7.1, 6.8, 2.7 Hz, CH$_3$CH$_3$CHCH), 4.25 (1H, b, CHCHOH), 5.16 (1 H, b, CHCHOH), 7.29–7.84 (8H, m, 6-H, 7-H, 8-H (Q), 5H (Ph)) and 8.06 (1H, d, J 7.87 Hz, 5-H(Q)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.8, 20.6, 25.0, 30.9, 65.1, 73.1, 120.8, 126.5, 126.7, 127.1, 129.2, 129.5, 133.2, 133.8, 135.5, 144.9, 158.1 and 160.0. Elemental analysis calculated for $C_{22}H_{27}N_3O_3S$: C, 63.90; H, 6.58; N, 10.16; S, 7.75%. Found: 63.85; H, 6.57; N, 9.80, S, 7.53%.

Sulfoximination of phenyl *tert*-butyl sulfoxide using Q^3NH_2

General procedure 1 was followed using Q^3NH_2 **30** (500 mg, 2.025 mmol), LTA (1.8 g, 3.036 mmol), HMDS (653 mg, 4.05 mmol) and phenyl *tert*-butyl sulfoxide **16d** (552 mg, 3.036 mmol) in a solution in dichloromethane (10 cm^3) to give sulfoximine **36**. The crude product contained a 1 : 1 ratio of sulfoximine diastereoisomers from comparison of signals at δ 5.33 and 5.50 ppm in its NMR spectrum (see below). The crude product was then chromatographed using column chromatography eluting with hexane–ethyl acetate 4 : 1 gave one sulfoximine diastereoisomer **36a** (R_f 0.3). The product crystallised on addition of ethanol to give as a colourless solid (329 mg, 34%) mp 133–135 °C (from ethanol). $[\alpha]_D$ = +39.7 (c = 0.42, $CHCl_3$), IR (in CH_2Cl_2 solution) $\nu_{max/}$ cm^{-1}: 3482 w, 3065 w, 2972 w, 2868 w, 1682 s, 1608 w, 1587 m and 1567m. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.06 (9H, s, (CH_3)$_3$CCH)), 1.56 (9H, s, (CH_3)$_3$CS)), 3.65 (1H, d, J 8.7 Hz, (CH$_3$)$_3$CCHOH)), 5.50 (1H, d, J 6.95 Hz, (CH$_3$)$_3$CCHOH)) and 7.27–8.19 (9H, m, 5-H, 6-H, 7-H, 8-H (Q), 5H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 24.6, 26.2, 38.1, 63.3, 74.4, 121.7, 126.2, 126.8, 127.0, 128.5, 131.8, 133.7, 134.9, 145.2, 160.8 and 160.9. Elemental analysis calculated for $C_{23}H_{30}N_3O_3S$: 64.46; H, 7.06; N, 9.80; S, 7.48%. Found: 64.15; H, 7.17; N, 9.65, S, 7.73%.

Further elution with the same solvent mixture gave sulfoximine **36b** diastereoisomer (R_f 0.22) as an oil (329 mg, 34%). $[\alpha]_D$ = +215.6 (c = 1.22, $CHCl_3$) IR (in CH_2Cl_2 solution) $\nu_{max/}$ cm^{-1}: 3472 w, 3065 w, 2953 w, 2868 w, 1681 s, 1589 m and 1567m. (Found: MH^+ 428.2001. $C_{23}H_{30}N_3O_3S$ requires M 428.2008), ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.03 (9H, s, (CH_3)$_3$CCH)), 1.49 (9H, s, (CH_3)$_3$CS)), 3.63 (1H, b, (CH$_3$)$_3$CCHOH)), 5.33 (1H, b, (CH$_3$)$_3$CCHOH)) and 7.25–8.05 (9H, m, 5-H, 6-H, 7-H, 8-H (Q), 5H (Ph)). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.0, 26.2, 37.7, 65.3, 74.6, 121.1, 126.5, 126.9, 127.1, 128.5, 129.3, 130.1, 133.6, 133.7, 145.1, 158.9 and 160.2.

General procedure 2 for the reaction of aldehydes with Et_2Zn in the presence of sulfoximine 34

Under argon atmosphere, to ligand **34** (20.4 mg, 0.0472 mmol) in dry Et_2O (0.5 ml) in a oven dried 10 ml round bottom flask was added Et_2Zn (1 ml, 1 M hexane solution) at room temperature in one portion and the solution stirred for 45 min. A solution of Ti(OPr^i)$_4$ (34 mg, 0.12 mmol) in Et_2O (0.5 ml) was then syringed into the reaction flask and with stirring for a further for 45 min. The reaction mixture was then cooled to –40 °C. After 5 min., freshly distilled aldehyde (0.472 mmol) solution in Et_2O (0.5 ml) was added and the reaction mixture was stirred for 24 h at –40 °C. The reaction mixture was quenched with saturated ammonium chloride and extracted with CH_2Cl_2. The organic phase was dried with anhydrous Na_2SO_4, filtered and concentrated. The enantiomeric purity of the product was determined by GC. The absolute configurations of the products were assigned by comparison with literature values.

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