Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

Addition-substitution reactions of 2-thio-3-chloroacrylamides with carbon, nitrogen, oxygen, sulfur and selenium nucleophiles

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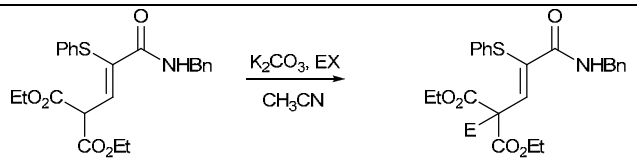
Carbon Based Nucleophiles

Alkylation of malonate adducts

Alkylation of the malonate adducts can be envisaged at either the α- or γ-position, and a brief exploration was undertaken to establish the potential synthetic utility of this transformation. Thus, **2c** was treated with allyl bromide, benzyl bromide and methyl iodide in the presence of potassium carbonate in acetonitrile. Table 1 summarises the results.

*Table 1 Alkylation of **2c***



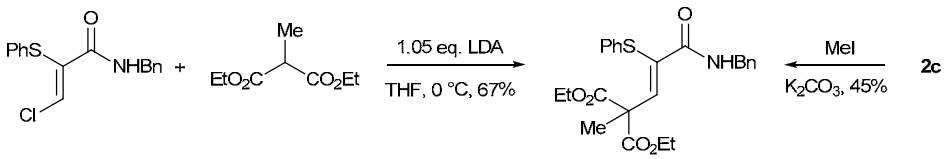
2c

EX	Product	% Yield[a]
allyl bromide	**3a**	27
benzyl bromide	**3b**	36

methyl iodide	**3c**	45

a) Isolated yield after chromatographic purification

To confirm that γ-alkylation had occurred, **3c** was independently synthesised by reacting diethyl 2-methylmalonate with **1c**, the spectroscopic details of which were identical to those of **3c** when prepared from the methylation of the diethyl malonate substituted acrylamide **2c** (Scheme 1).



Scheme 1

Nitrogen Based Nucleophiles

Examination of the X-ray structure of **24a** reveals the existence of a hydrogen bond from the amide proton to an oxygen of the sulfone, leading to a highly organised and rigid six-membered structure (Figure 1).

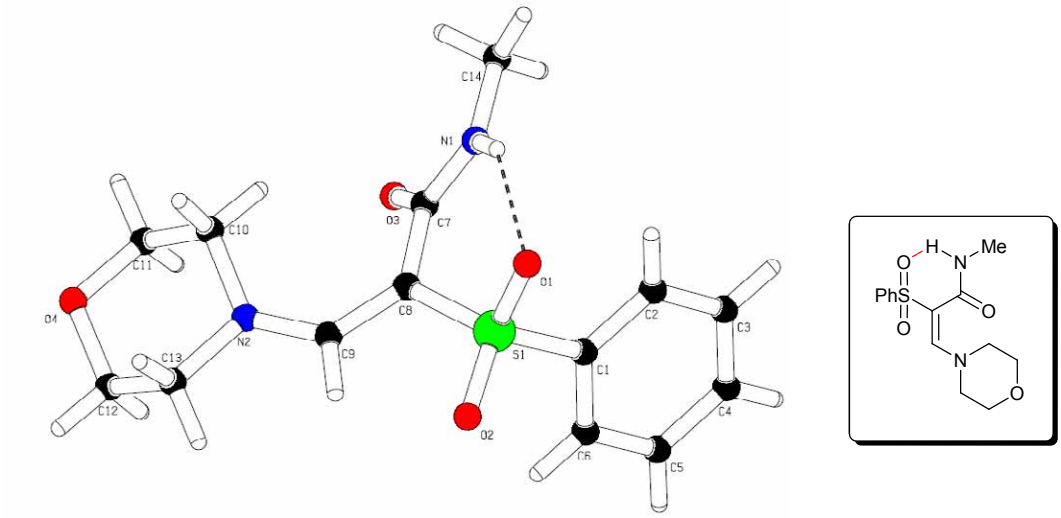


Figure 1

Interestingly, analysis of the dihedral angles outlined in Table 2 reveal that the acrylamide unit is quite distorted from planarity, reflecting limited conjugation between nitrogen and the acrylamide system. However, this isomer is clearly more stable than the analogous *Z* isomer, which was never observed.

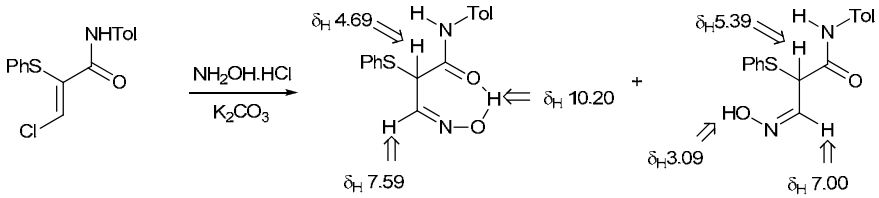
*Table 2 Selected Dihedral Angles in **24a***

	Dihedral Angle
O3-C7-C8-C9	–37.4
N1-C7-C8-C9	143.3
N2-C9-C8-C7	–14.9
C10-N2-C8-C9	–12.9
C13-N2-C8-C9	–174.2

Reaction with ammonia and hydroxylamine

Treatment of the sulfide **1a** with ammonia and hydroxylamine resulted in complex mixtures of products due to the possibilities for *E* and *Z* isomer formation and imine-amine tautomerisation.

Treatment of the sulfide **1a** with hydroxylamine (generated *in situ* from hydroxylamine hydrochloride and potassium carbonate) yielded two products, tentatively assigned as the oxime isomers **29a** (Scheme 2). However, due to interconversion of the *E* and *Z* isomers, these were not isolated or fully characterised.



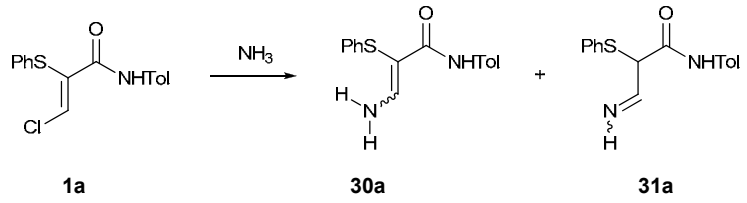
1a **29a**-*E* **29a**-*Z*

Scheme 2

While full characterisation was not possible, two pairs of doublets at δ_H 4.69 and 7.59 (*J* 8) for the isomer tentatively assigned as *Z*, and at δ_H 5.39 and 7.00 (*J* 8) for the isomer tentatively assigned as *E*, characteristic of the oxime were evident in the ^{1}H NMR spectrum. Tentative stereochemical assignment of the *E* isomer was made on the basis that the ^{1}H NMR spectrum showed a broad OH signal at δ_H 10.11-10.27, deshielded due to intramolecular hydrogen-bonding, while the other isomer had an OH signal at δ_H 3.09. The ratio of the *E* and *Z* oximes was determined in several solvents and was estimated by ^{1}H NMR integration of

the α and β-protons. In acetone-d_6 and DMSO-d_6, the *Z* isomer was favoured (1.4:1) while they were equally abundant in d_4-methanol (1:1).

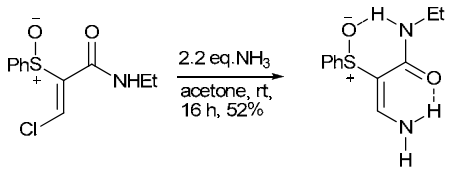
On reaction of **1a** with 2.2 equivalents of aqueous ammonia in acetone, the reaction was incomplete by TLC analysis after 74 hours and a further 2.2 equivalents of aqueous ammonia was added. After stirring at room temperature for a further 24 hours, only traces of the sulfide **1a** remained and following the work-up, a mixture of isomers of the ammonia adduct, tentatively assigned as the *E* and *Z* isomers and potentially containing imino tautomers, was obtained. Chromatographic purification proved complex as equilibration of the *E* and *Z* isomers and tautomers made isolation difficult. Thus, the isomers were not isolated or fully characterised but were tentatively assigned as *E* and *Z* isomers of the β-aminoacrylamide **30a** and β-iminoacrylamide **31a** (Scheme 3).



1a **30a** **31a**

Scheme 3

In contrast, reaction of the sulfoxide **18c** with 2.2 equivalents of aqueous ammonia in acetone gave the adduct **32c** as a single stereoisomer (tentatively assigned as *E*) following stirring at room temperature for 16 hours (Scheme 4). The extended conjugation with the sulfoxide favours the enamino tautomer, with no evidence for the analogous imino tautomer at the sulfoxide level of oxidation.



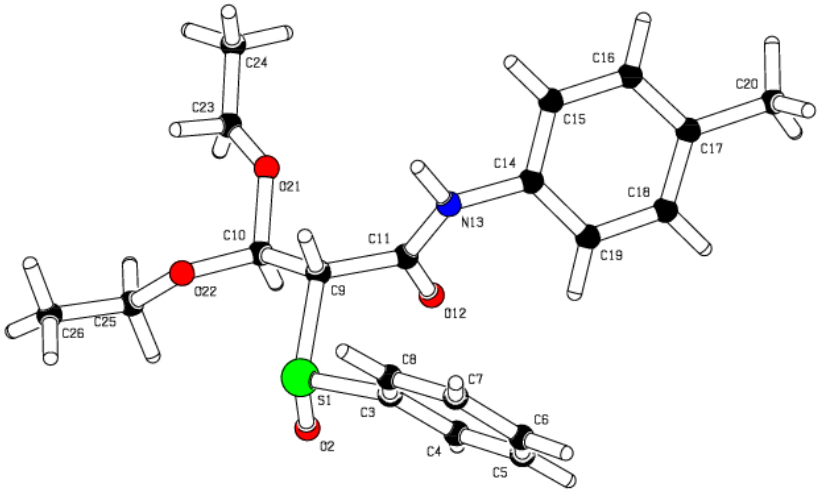
18c **32c**

Scheme 4

The observation of only one stereoisomer of **32c** can be rationalised in terms of stabilisation of the enamino adduct by intramolecular hydrogen bonding. The ^{1}H NMR spectroscopic evidence supports the *E* isomer assignment, with the signal for the β-hydrogen in the range δ_H 7.29-7.62, and one enamine proton involved in hydrogen hydrogen bonding being more deshielded (δ_H 7.27) than the other non-hydrogen bonded proton (δ_H 5.38).

Oxygen Based Nucleophiles

The relative stereochemistry of the major isomer of the acetal **38a** was determined by single crystal X-ray diffraction after recrystallisation of a sample from acetonitrile/acetone (Figure 2).



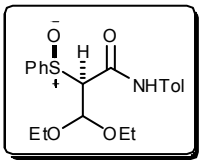


Figure 2

Experimental

Carbon Nucleophiles

Addition of enolate of diethyl malonate

(1*S*)-*N*-1-Phenylethyl-4,4-di(ethoxycarbonyl)-2-(phenylthio)-2-pentenamide 2b

This was prepared following the procedure described for pentenamide **2a** using DIPA (73 mg, 0.7 mmol), *n*-butyllithium (0.3 mL, 1.6 M in hexane, 0.69 mmol), diethylmalonate (101 mg, 0.7 mmol), **1b** (0.20g, 0.63 mmol) and THF (5 and 5 mL) at 0 °C for 1 h and then at 10 °C for 1 h. Purification by chromatography using ethyl acetate-hexane (20:80) as eluent gave **2b** (0.20 g, 72%) as a colourless oil. The product contained a minor isomer which could not be separated by chromatography. The ratio was estimated to be (30:1) by ^{1}H NMR integration; $[\alpha]_{20}^{D}$ –0.37 (*c* 9 in ethanol); (Found C, 64.80; H, 6.22; N, 3.11. $C_{24}H_{27}NO_5S$ requires C, 65.29; H, 6.16; N, 3.17%); ν_{max}/cm^{-1} (film) 3339 (br NH), 1747 (CO ester), 1643 (CO α,β-unsaturated amide); δ_H (270 MHz, $CDCl_3$) 1.27 (9H, m, 2 × C*H*$_3$CH$_2$O and C*H*$_3$CHPh), 4.11, 4.29 (4H, m, 2 × C*H*$_2$O), 4.90 [1H, d, *J* 10, C(4)*H*], 4.96-5.05 (1H, dq, *J* 7, 8, NC*H*), 6.90-7.30 (10H, m, Ar*H*), 7.60 [1H, d, *J* 10, C(3)*H*=]; δ_C (67.8 MHz, $CDCl_3$) 13.9 (*C*H$_3$CH$_2$O), 21.3 (*C*H$_3$CHPh), 49.3 (N*C*H), 54.2 [*C*(4)H], 64.2 (*C*H$_2$O) 125.8, 127.0, 127.1, 128.1, 128.5, 129.5 (aromatic *C*H), 132.4, 133.5 (quaternary aromatic *C* and S*C*=), 139.7 [*C*(3)H=], 142.5 (quaternary aromatic *C*), 162.0 (*C*O amide), 166.4 (*C*O ester); MS *m/z* 441 (M^+, 23%), 395 (17%, M^+-EtOH), 291 (30%), 120 (22%), 105 (100%); Signals for the minor isomer were seen in the ^{1}H NMR spectrum at 5.40 [1H, d, *J* 9, C(4)*H*], 6.78 [1H, d, *J* 10, C(3)*H*=]; all other signals were identical to the major isomer.

***N*-Benzyl-4-ethoxycarbonyl-2-(phenylthio)-2-pentenamide-5-ethylester 2c**

This was prepared following the procedure described for pentenamide **2a** using DIPA (0.5 mL, 3.6 mmol), *n*-butyllithium (2.4 mL, 1.6 M in hexane, 3.8 mmol), diethylmalonate (0.6 mL, 3.6 mmol), **1c** (1.00 g, 3.3 mmol) and THF (20 and 15 mL) at 0 °C. Following stirring at room temperature for 1.5 h, the crude product was obtained as an orange oil. Following chromatography on silica gel using 20:80 ethyl acetate/hexane the pure product **2c** was isolated as a white solid (1.25 g, 88%); m.p. 82−84 ^{o}C; (Found C, 64.81 ; H, 5.92; N, 3.27; S, 7.81; $C_{23}H_{25}NO_5S$ requires C, 64.62; H, 5.89; N, 3.28; S, 7.50%) ; ν_{max}/cm^{-1} (film) 3331

(NH), 1750, 1734 (CO ester), 1649 (CO amide); δ_H (400 MHz, $CDCl_3$) 1.27 (6H, t, *J* 7.3, 2 × C*H*$_3$), 4.22 (4H, q, *J* 7.0, 2 × C*H*$_2$), 4.40 (2H, d, *J* 5.9, NC*H*$_2$Ph), 4.91 [1H, d, *J* 9.7, C*H*$(CO_2Et)_2$], 6.83-6.91 (2H, m, Ar*H*), 7.06-7.33 (9H, m, Ar*H*, N*H*), 7.67 [1H, d, *J* 9.7, C(3)*H*=]; δ_C (100.6 MHz, $CDCl_3$) 14.4 (CH_3, OCH_2CH_3), 44.5 (CH_2, NCH_2Ph), 54.6 [CH, *C*H$(CO_2Et)_2$], 62.5 (CH_2, OCH_2CH_3), 127.3, 127.7, 128.4, 128.9, 129.1, 129.9 (CH, aromatic *C*H), 132.5, 133.9, 137.9 (C, 2 × aromatic *C*, PhS*C*=), 140.7 [CH, *C*(3)H=],163.5 (C, amide *C*O), 166.8 (C, ester *C*O); MS *m/z* 427 (11%, M^+), 268 [7%, $(M–C_7H_{11}O_4)^+$], 91 [100%, $(CH_2Ph)^+$]. There is some evidence, including TLC evidence, that this compound is interconverting with a minor isomer in a 15:1 ratio; δ_H (270 MHz, $CDCl_3$) 4.38 (2H, d, *J* 5.9, NC*H*$_2$Ph), 5.49 [1H, d, *J* 9.7, C*H*$(CO_2Et)_2$], 6.82 [1H, d, *J* 9.7, C(3)*H*=].

Alkylation

N-phenylmethyl-4,4-di(ethoxycarbonyl)-5-phenyl-2-phenylthio-2-pentenamide 3b

Following the procedure described for the synthesis of **3a**, using **2c** (0.30 g, 0.69 mmol), potassium carbonate (0.19 g, 1.39 mmol) and benzyl bromide (0.17 mL, 1.39 mmol) in acetonitrile (6 mL) and acetone (3 mL), a mixture of products was recovered. Following chromatography on silica gel using 15:85 ethyl acetate/hexane as eluent, **3b** was isolated as a white solid (0.13 g, 36%), and subsequently recrystallised from ether; mp 109−111 °C; (Found C, 69.80; H, 6.13; N, 2.92; S, 5.85; $C_{30}H_{31}NO_5S$ requires C, 69.61; H, 6.04; N, 2.71; S, 6.19 %); ν_{max}/cm^{-1} (KBr) 3352 (NH), 1733 (CO ester), 1650 (CO amide); δ_H (300 MHz, $CDCl_3$) 1.23-1.30 (6H, 2 × overlapping t, *J* 7.1, 2 × OCH_2CH_3), 3.43-3.53 [2H, ABq, *J* 13.7, C(5)*H*$_2$], 4.04-4.42 (6H, m, NC*H*$_2$Ph, 2 × OCH_2CH_3), 6.85-6.98 (3H, m, Ar*H*), 7.13-7.30 (13H, m, Ar*H*, N*H*), 7.57 [1H, s, C(3)*H*=]; δ_C (75.5 MHz, $CDCl_3$) 13.9, 14.1 (CH_3, 2 × OCH_2CH_3), 44.5, 45.4 [CH_2, NCH_2Ph, *C*(5)H_2], 60.9 [C, *C*(4)], 61.5, 61.7 (CH_2, 2 × OCH_2CH_3), 127.49, 127.52, 128.0, 128.08, 128.13, 128.6, 128.9 (CH, aromatic *C*H), 129.1 (C, =*C*SPh), 130.7 (CH, aromatic *C*H), 131.1 (C, aromatic *C*), 132.2 (CH, aromatic *C*H), 134.6, 137.1 (C, aromatic *C*), 144.9 [CH, *C*(3)H=], 163.8 (C, amide *C*O), 166.5, 168.5 (C, 2 × *C*O ester); MS *m/z* 426 [2%, $(M\text{-}CH_2Ph)^+$], 110 (93%, HSPh), 77 [80%, $(C_6H_5)^+$], 43 [87%, $(CONH)^+$].

N-Phenylmethyl-4,4-di(ethoxycarbonyl)-2-phenylthio-2-pentenamide 3c

Method A

The title compound was prepared following the procedure described for **3a**, using **2c** (0.44 g, 1.03 mmol), potassium carbonate (0.28 g, 2.06 mmol) and methyl iodide (0.13 mL, 2.06 mmol) in acetonitrile (6 mL) and acetone (3 mL). Following chromatography on silica gel using 15:85 ethyl acetate/hexane as eluent, the product **3c** was recovered as a solid (0.08 g) containing an impurity; mp 91−93 °C; δ_H (300 MHz, $CDCl_3$) 1.21 (8H, t, *J* 7.1, 2 × OCH_2CH_3, 2H due to overlapping impurity), 1.70 (3H, s, CH_3), 3.44-3.51 (1.4H, q, *J* 7.0, impurity), 4.01-4.22 (4H, 2 × sym. m, 2 × OCH_2CH_3), 4.36 (2H, d, *J* 5.9, NCH_2Ph), 6.74-6.79 (2H, m, Ar*H*), 6.96-7.31 (9H, m, Ar*H*, N*H*), 7.93 [1H, s, C(3)*H*=]; δ_C (75.5 MHz, $CDCl_3$) 13.9 (CH_3, OCH_2CH_3), 15.3 (CH_3, Impurity), 22.7 [CH_3, *C*(5)H_3], 44.1 (CH_2, NCH_2Ph), 56.3 [C, *C*(4)], 62.2 (CH_2, OCH_2CH_3), 65.9 (CH_2, impurity), 126.6, 127.2, 127.3, 128.5, 128.7, 129.4 (CH, aromatic *C*H), 133.8, 137.5 [C, =*C*(2), aromatic *C*], 147.4 [CH, *C*(3)H=], 163.7 (C, amide *C*O), 170.1 (C, ester *C*O); MS *m/z* 441 [7%, $(M)^+$], 368 [4%, $(M\text{-}CO_2Et)^+$], 135 [30%, $(CONHCH_2Ph)^+$], 106 [57%, $(NHCH_2Ph)^+$], 91 [75%, $(CH_2Ph)^+$], 43 [100%, $(CONH)^+$].

Method B

Diisopropylamine (0.25 mL, 0.18 g, 1.82 mmol) was dissolved in THF (10 mL) and cooled to 0 °C under nitrogen. *n*-Butyllithium (1.6 M solution in hexanes, 0.86 mL, 1.90 mmol) was added dropwise and the mixture was stirred for 20 min while warming to room temperature. Diethyl 2-methyl-malonate (0.28 mL, 1.80 mmol) was added and the mixture was stirred for a further 20 min. A solution of **1c** (0.53 g, 1.65 mmol) in THF (8 mL) was slowly added and stirring was continued for 1.5 h. The reaction was quenched with saturated aqueous ammonium chloride (10 mL), CH_2Cl_2 (25 mL) was added and the phases were separated. The aqueous layer was washed with CH_2Cl_2 (2 × 10 mL) and the combined organic layers were washed with a saturated solution of sodium bicarbonate (2 × 10 mL) and brine (2 × 10 mL), dried and concentrated under reduced pressure to give the crude product as a white solid. Following purification by column chromatography using hexane:ethyl acetate (80:20) as eluent, **3c** was obtained as a white solid (0.44 g, 67%), with spectroscopic details identical to those outlined above.

Addition of enolate of ethyl acetoacetate

N-(4-Methylphenyl)-4-ethoxycarbonyl-2-(phenylthio)-2-butenamide 5a

This was prepared following the procedure described for pentenamide **4a** using DIPA (0.19 g, 1.90 mmol), *n*-butyllithium (0.73 mL, 1.6 M in hexane, 1.82 mmol), ethyl acetoacetate (0.24 g, 1.82 mmol), β-chloroacrylamide **1a (**0.5 g, 1.65 mmol) and THF (20 mL). The

reaction was complete after stirring at 0 °C for 1 h followed by 4 h at room temperature. Purification by chromatography using ethyl acetate-hexane (15:85) as eluent gave β-chloroacrylamide **1a** (64 mg, 13%) and **5a** (0.13 g, 22%) as a colourless oil; ν_{max}/cm^{-1} (film) 3375 (br NH), 1738 (CO ester), 1675 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.26 (3H, t, *J* 7, C*H*$_3$CH$_2$O), 2.28 (3H, s, ArC*H*$_3$), 3.60 [2H, d *J* 7, C(4)*H*$_2$], 4.18 (2H, q, *J* 7, C*H*$_2$O), 7.06-7.40 (9H, m, Ar*H*), 7.80 [1H, t, *J* 7, C(3)*H*=], 8.72 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 14.2 (CH_3, *C*H$_3$CH$_2$O), 20.9 (CH_3, Ar*C*H$_3$), 36.6 [CH_2, *C*(4)H$_2$], 61.3 (CH_2, *C*H$_2$O), 120.2, 126.9, 127.5, 129.5, 129.6 (CH, aromatic *C*H), 129.9, 133.7, 134.4, 134.9 (4 × C, quaternary aromatic *C* and S*C*=), 143.7 [CH, *C*(3)H=], 161.5, 169.5 (2 × C, *C*O amide, *C*O ester).

Addition of enolate of cyclohexanone

N-(4-Methylphenyl)-3-(2-oxocyclohexyl)-2-(phenylthio)propenamide 6a

This was prepared following the procedure described for pentenamide **2a** using DIPA (50 μl, 0.36 mmol), *n*-butyllithium (0.16 mL, 1.6 M in hexane, 0.38 mmol), cyclohexanone (38 μl, 0.36 mmol), β-chloroacrylamide **1a** (100 mg, 0.33 mmol) and THF (4 mL). The reaction was complete after 10 min. Purification by chromatography using ethyl acetate-hexane (20:80) as eluent gave **6a** (61 mg, 51%) as a white, crystalline solid; mp 164−166°C; (Found C, 72.08; H, 6.53; N, 3.81; S, 8.52. $C_{22}H_{23}NO_2S$ requires C, 72.30; H, 6.34; N, 3.83; S, 8.77%); ν_{max}/cm^{-1} (KBr) 3364 (br NH), 1702 (CO ketone), 1674 (CO α,β-unsaturated amide); δ_H (270 MHz, $CDCl_3$) 1.68-1.82 [2H, m, C(4)*H*$_2$ or C(5)*H*$_2$], 2.05-2.19 [2H, m, C(4)*H*$_2$ or C(5)*H*$_2$], 2.28 (3H, s, ArC*H*$_3$), 2.28-2.42 [2H, m, C(3)*H*$_2$], 2.44-2.58 [2H, m, C(6)*H*$_2$], 3.73-3.89 [1H, m, C(2)*H*], 7.05-7.31 (9H, m, Ar*H*), 7.73 [1H, d, *J* 9, C(3)*H*=], 8.63 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 21.2 (CH_3, Ar*C*H$_3$), 24.3, 27.3, 33.6, 42.1 [CH_2, *C*(3)H$_2$, *C*(4)H$_2$, *C*(5)H$_2$, *C*(6)H$_2$], 53.5 [CH, *C*(2)H], 120.5, 127.1, 127.6 (CH, aromatic *C*H), 129.0 (C, aromatic *C* or S*C*=), 129.91, 129.94, (2 × CH, aromatic *C*H), 134.2, 134.4, 135.3 (3 × C, aromatic *C*), 149.1 [CH, *C*(3)H=], 161.8 (C, *C*O amide), 208.8 [C, *C*(1)O]; MS *m/z* 365 (M^+, 7 %), 189 (27%), 135 (100%).

Addition of nBu$_2$CuLi

N-Benzyl-2-(phenylthio)-*Z*-2-heptenamide 7c

This was prepared following the procedure described for **7a** using CuI (0.25 g, 1.32 mmol), *n*-butyllithium (1.7 mL, 1.6 M solution in hexanes, 2.64 mmol), **1c** (0.20 g, 0.66 mmol) and ether (25 mL and 20 mL) at –78 °C. Following 2.5 hours reaction time, during which the temperature

was maintained at –78 °C for 1 h and then allowed to warm slowly to room temperature, the crude product was shown to contain a complex mixture of compounds. These were separable by column chromatography on silica gel, using 30:70 ethyl acetate/hexane as eluent. The initial fraction consisting of mixed side-products was shown to be mainly diphenyldisulphide by ^{1}H spectroscopy. The minor *E* isomer of the addition product, **7c**-*E*, was recovered in trace amounts (0.01g, <3%); δ_H (270 MHz, $CDCl_3$) 0.94 [3H, t, *J* 7.0, C(7)H_3], 1.24-1.65 [4H, m, C(6)H_2, C(5)H_2], 2.65-2.81 [2H, m, C(4)H_2], 4.36 (2H, d, *J* 5.9, NCH_2Ph), 6.66 [1H, t, *J* 7.6, C(3)*H*=], 6.84-6.90 (2H, m, Ar*H*), 6.98 (1H, br s, N*H*), 7.08-7.41 (8H, m, Ar*H*). **7c**-*Z* was recovered as a white solid (0.07 g, 34%) containing a trace of **1c**. This was recrystallised from ether; mp 79−81 °C; (Found C, 74.30; H, 7.06; N, 4.35; $C_{20}H_{23}NOS$ requires C, 73.80; H, 7.12; N, 4.30%); ν_{max}/cm^{-1} (KBr) 3362 (NH), 1645 (CO), 1605, 1582 (C=C), 1515; δ_H (300 MHz, $CDCl_3$) 0.89 [3H, t, *J* 7.2, C(7)H_3], 1.22-1.54 [4H, m, C(6)H_2, C(5)H_2], 2.45-2.56 [2H, m, C(4)H_2], 4.41 (2H, d, *J* 5.9, NCH_2Ph), 6.85-6.94 (2H, m, Ar*H*), 7.18-7.32 (9H, m, Ar*H*, N*H*), 7.66 [1H, t, *J* 7.5, C(3)*H*=]; δ_C (75.5 MHz, $CDCl_3$) 13.8 [CH_3, *C*(7)H_3], 22.5 [CH_2, *C*(6)H_2], 30.5, 30.6 [CH_2, *C*(4)H_2 and *C*(5)H_2], 43.9 (CH_2, N*C*H_2), 125.8 (C, aromatic *C*), 126.1, 126.9, 127.16, 127.19, 128.5, 129.3 (CH, aromatic *C*H), 135.1, 137.9 [C, aromatic *C*, *C*(2) =], 153.1 [CH, *C*(3)H=], 164.3 (C, *C*O); MS *m/z* 325 (M^+, 14%), 268 [5%, (M-C_4H_9)$^+$], 191 [6%, (268-C_6H_5)$^+$], 106 [24%, (NCH_2Ph)$^+$], 91 [100%, (CH_2Ph)$^+$], 77 [19%, (C_6H_5)$^+$]. The desulfinylation product *N*-benzyl-2-heptenamide **8c** (*trans*) was also recovered (0.03 g, 24%) as a yellow oily solid; (Found C, 77.80; H, 8.45; N, 6.00; $C_{14}H_{19}NO$ requires C, 77.38; H, 8.81; N, 6.45%); ν_{max}/cm^{-1} (film) 3281 (NH), 2957, 2927 (CH), 1668 (CO), 1633 (C=C); δ_H (270 MHz, $CDCl_3$) 0.90 [3H, t, *J* 7.0, C(7)H_3], 1.20-1.55 [4H, m, C(5)H_2, C(6)H_2], 2.13-2.25 [2H, m, C(4)H_2], 4.50 (2H, d, *J* 5.7, NCH_2Ph), 5.73-5.86 [2H, br s. overlapping dt, *J* 15.1, 1.4, C(2)*H*=, N*H*], 6.82-6.95 [1H, dt, *J* 15.1, 7.0, C(3)*H*=], 7.15-7.42 (5H, m, Ar*H*); δ_C (67.8 MHz, $CDCl_3$) 13.8 [CH_3, *C*(7)H_3], 22.2 [CH_2, *C*(6)H_2], 30.3 [CH_2, *C*(5)H_2], 31.8 [CH_2, *C*(4)H_2], 43.6 (CH_2, N*C*H_2Ph), 123.2 [CH, =*C*(2)H], 127.5, 127.9, 128.7 (CH, aromatic *C*H), 145.4 (C, aromatic *C*), 145.4 [CH, C(3)H=], 166.0 (C, *C*O); MS *m/z* 217 (M^+, 40%), 188 [23%, (M-C_2H_5)$^+$], 160 [70%, (M-C_4H_9)$^+$], 106 [43%, (NCH_2Ph)$^+$], 91 [90%, (CH_2Ph)$^+$], 57 [79%, (C_4H_9)$^+$], 43 [100%, (CONH)$^+$].

N,N-Dimethyl-2-(phenylthio)-2-heptenamide 7d

This was prepared following the procedure described for **7a** using CuI (0.32 g, 1.65 mmol), *n*-butyllithium (2.1 mL, 1.6 M solution in hexanes, 3.30 mmol), **1d** (0.20 g, 0.83 mmol) and ether (25 mL and 20 mL) at –78 °C over 3.5 h. Following column chromatography on silica gel using

4:1:5 ethyl acetate/dichloromethane/hexane, the minor *E* isomer of the adduct, **7d**-*E*, was recovered as an oil (0.002 g, 1%); δ_H (270 MHz, $CDCl_3$) 0.85-0.96 [3H, m, C(7)H_3], 1.24-1.43 [4H, m, C(6)H_2, C(5)H_2], 2.05-2.16 [2H, m, C(4)H_2], 2.89, 2.86 (6H, 2 × s, N(CH_3)$_2$], 5.91 [1H, t, *J* 7.6, C(3)*H*=], 7.18-7.33, 7.40-7.53 (5H, 2 × m, Ar*H*). It is worth noting that this does not significantly isomerise to the *Z* form (~ 5%), even after 18 months at room temperature. The Z adduct **7d**-*Z* was recovered as an oil (0.07 g, 34%); δ_H (270 MHz, $CDCl_3$) 0.88-0.98 [3H, m, C(7)H_3], 1.26-1.52 [4H, m, C(6)H_2, C(5)H_2], 2.32-2.44 [2H, m, C(4)H_2], 2.70, 2.92 (6H, 2 × br s, N(CH_3)$_2$], 6.09 [1H, t, *J* 7.3, C(3)*H*=], 7.19-7.50 (5H, m, Ar*H*). This fraction also contained a tiny trace of the *E* isomer, **7d**-*E*, and a trace of the starting material **1d**. A final fraction containing both *cis*- and *trans*- isomers of the desulphinylation product **8d**, in a 1:1 ratio, was also recovered as an oil (0.03 g, 23%); δ_H (270 MHz, $CDCl_3$) 0.87-0.96 [6H, m, C(7)H_3], 1.25-1.51 [8H, m, C(6)H_2, C(5)H_2], 2.14-2.25 [2H, m, C(4)H_2 (*trans*)], 2.29-2.40 [2H, m, C(4)H_2 (*cis*)], 3.00, 3.04 [12H, 2 × s, N(CH_3)$_2$], 5.82-6.00 [2H, m, C(2)*H*= (both *cis* and *trans*)], 6.20-6.28 [1H, dt, *J* 14.9, 1.6, C(3)*H*= (*cis*)], 6.82-6.93 [1H, dt, *J* 15.1, 6.7, C(3)*H*= (*trans*)].

_N_-Ethyl-2-(phenylthio)-2-heptenamide 7e

This was prepared following the above procedure for the synthesis of **7a**, from **1e** (0.24 g, 0.99 mmol), CuI (0.38 g, 1.99 mmol) and *n*-butyllithium (1.6 M in hexanes, 2.5 mL, 3.99 mmol) in ether (40 mL), over 2.5 hours at –78 °C. Following purification by column chromatography on silica gel using 12:88 ethyl acetate/hexane as eluent, an initial fraction was recovered (0.006 g) containing a mixture of compounds, one of which has been tentatively identified as **9e**; δ_H (270 MHz, $CDCl_3$) 2.12-2.24 [1H, m, C*H*(Bu)$_2$], 3.81 (1H, d, *J* 4.1, C*H*SPh). The *Z* adduct, **7e**-*Z*, was recovered as an oil (0.04 g, 15%); ν_{max}/cm^{-1} (film) 3329 (NH), 1651 (CO), 1608, 1583 (C=C), 1517; δ_H (270 MHz, $CDCl_3$) 0.88 [3H, t, *J* 7.0, C(7)H_3], 0.97 (3H, t, *J* 7.4, NCH$_2$CH_3), 1.24-1.52 [4H, m, C(6)H_2, C(5)H_2], 2.42-2.53 [2H, m, C(4)H_2], 3.19-3.32 (2H, m, NCH_2), 6.96 (1H, br s, N*H*), 7.10-7.34 (5H, m, Ar*H*), 7.62 [1H, t, *J* 7.6, C(3)*H*=]; δ_C (67.8 MHz, $CDCl_3$) 13.8 [CH_3, *C*(7)H$_3$], 14.5 (CH_3, NCH$_2$*C*H$_3$), 22.5 [CH_2, *C*(6)H$_2$], 30.5, 30.6 [CH_2, *C*(5)H$_2$, *C*(4)H$_2$], 34.9 (CH_2, N*C*H$_2$), 126.0 (CH, aromatic *C*H), 126.9 (C, aromatic *C* or =*C*SPh), 127.1, 129.5 (CH, aromatic *C*H), 135.4 (C, aromatic *C* or =*C*SPh-), 152.5 [CH, *C*(3)H=], 164.2 (C, *C*O); MS *m/z* 263 (M^+, 75%), 154 [32%, $(M\text{-PhS})^+$], 109 [35%, $(PhS)^+$], 72 [94%, $(CONHEt)^+$], 43 [100%, $(CONH)^+$].

***N*-*i*-Propyl-2-(phenylthio)-2-heptenamide 7f**

This was prepared following the above procedure for the synthesis of **7a**, using **1f** (0.40 g, 1.57 mmol), CuI (0.60 g, 3.14 mmol) and *n*-butyllithium (1.6 M in hexanes, 3.9 mL, 6.27 mmol) in ether (55 mL) over 2.25 hours at –78 °C. Following column chromatography on silica gel using 12:88 ethyl acetate/hexane as eluent, an initial fraction containing a mixture of impurities, including diphenyldisulphide was recovered. The *Z* adduct, **7f**-*Z* was recovered as a clear oil (0.07 g, 15%); ν_{max}/cm^{-1} (film) 3310 (NH), 1660 (CO), 1609, 1584 (C=C), 1514; δ_H (300 MHz, $CDCl_3$) 0.89 [3H, t, *J* 7.2, C(7)*H*$_3$], 0.97 [6H, d, *J* 6.5, NCH(C*H*$_3$)$_2$], 1.27-1.52 [4H, m, C(6)*H*$_2$, C(5)*H*$_2$], 2.42-2.52 [2H, m, C(4)*H*$_2$], 3.92-4.08 (1H, septet, *J* 6.5, NC*H*), 6.72 (1H, br d, N*H*), 7.12-7.33 (5H, m, Ar*H*), 7.56 [1H, t, *J* 7.5, C(3)*H*=]; δ_C (75.5 MHz, $CDCl_3$) 13.8 [CH_3, *C*(7)H_3], 22.4 [CH_3, NCH(*C*H_3)$_2$], 22.5 [CH_2, *C*(6)H_2], 30.54 [2 × CH_2, *C*(5)H_2, *C*(4)H_2], 41.8 (CH, N*C*H), 126.1 (CH, aromatic *C*H), 126.30 (C, aromatic *C*), 127.1, 129.2 (CH, aromatic *C*H), 135.2 (C, aromatic *C*), 151.9 [CH, *C*(3)H=], 163.30 (C, *C*O); MS *m/z* 277 (M^+, 28%), 168 [12%, $(M\text{-}PhS)^+$], 57 [69%, $(C_4H_9)^+$], 43 [100%, $(CONH)^+$]. Another fraction (0.01 g) was recovered containing a complex mixture of side products, one of which was tentatively identified as the *E* isomer **7f**-*E* by the signal at δ_H 6.56 [1H, t, *J* 7.4, C(3)*H*=]. Another of these compounds has been tentatively identified as the diadduct **8f**; δ_H 2.10-2.24 [1H, m, C*H*(Bu)$_2$], 3.79 (1H, d, *J* 4.3, C*H*SPh).

***N*-(4-Methylphenyl)-3-methyl-2-(phenylthio)-*Z*-2-heptenamide 7g**

This was prepared following the procedure described for **7a** using cuprous iodide (0.25 g, 1.32 mmol), *n*-butyllithium (1.65 ml, 1.6 M in hexane, 2.64 mmol), **1g** (0.21 g, 0.66 mmol), and ether (25 and 10 ml). The reaction was complete by TLC analysis after 17 h. Purification by chromatography using ethyl acetate-hexane (5:95) as eluent gave **7g** (26 mg, 12%) as a white, crystalline solid, mp 89−91 °C; (Found C, 73.90; H, 7.28; N, 4.18; S, 9.09. $C_{21}H_{25}NOS$ requires C, 74.30; H, 7.42; N, 4.13; S, 9.44%); ν_{max}/cm^{-1} (KBr) 3255 (br NH), 1640, 1592 (CO α,β-unsaturated amide); δ_H (270 MHz, $CDCl_3$) 0.93 [3H, t, *J* 7, C(7)*H*$_3$], 1.33-1.55 [4H, m, C(6)*H*$_2$ and C(5)*H*$_2$], 2.26 (3H, s, ArC*H*$_3$), 2.29 (3H, s, C*H*$_3$CH=), 2.55-2.65 [2H, m, C(4)*H*$_2$], 7.02-7.31 (9H, m, Ar*H*), 8.31 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 13.9 [*C*(7)H_3], 20.8 (Ar*C*H_3), 21.8 (*C*H_3C=), 22.8 [*C*(6)H_2], 30.4 [*C*(5)H_2], 38.6 [*C*(4)H_2], 120.3 (aromatic *C*H), 121.7 (*C* or S*C*=), 126.3, 127.7, 129.3, 129.6 (aromatic *C*H), 133.9,

135.3, 135.4 (aromatic *C* or S*C*=), 159.0 (*C*=), 164.6 (*C*O); MS *m/z* 339 (M^+, 83 %), 282 (2%, M^+-Bu^n), 233 (19%, M^+-NH^{p}Tol), 205 (7%, M^+-CONH^{p}Tol).

Addition of Me_2CuLi

N-(4-Methylphenyl)-2-(phenylthio)-2-butenamide 10a

This was obtained following the procedure for **10c** using **1a** (0.38 g, 1.25 mmol), CuI (0.48 g, 2.50 mmol), and methyl lithium (3.1 mL, 1.6 M solution in ether, 4.99 mmol) in dry ether (50 mL) at –78 °C, for 2.5 hours reaction time. After chromatography on silica gel using 25:75 ethyl acetate/hexane as eluent, the initial fraction recovered contained starting material (9%) with a trace of **10a**. The pure product **10a** was recovered as a white solid (0.10 g, 30%); mp 100−101 °C; ν_{max}/cm^{-1} (film) 3434 (NH), 1652 (CO); δ_H (300 MHz, $CDCl_3$) 2.10 [3H, d, *J* 6.9, C(4)*H*$_3$], 2.27 (3H, s, ArC*H*$_3$), 7.03-7.38 (9H, m, Ar*H*), 7.82 [1H, q, *J* 6.9, =C*H*], 8.80 (1H, br s, N*H*).

(*S*)-*N*-(1-Phenylethyl)-2-(phenylthio)-2-butenamide 10b

This was obtained using **1b** (0.30 g, 0.95 mmol), CuI (0.36 g, 1.89 mmol) and methyl lithium (2.7 mL, 1.4 M in ether, 3.79 mmol) in ether (35 mL) for 2 h at –57 °C. The crude product mixture, containing a 1:2 ratio of starting material to *Z* adduct, was reacted with morpholine (~0.2 mL) to remove the excess starting material, giving after chromatography on silica gel using 20:80 ethyl acetate/hexane as eluent, the pure product **10b** as a yellow oil (0.12 g, 44%); ν_{max}/cm^{-1} (film) 3428 (NH), 1652 (CO); δ_H (300 MHz, $CDCl_3$) 1.32 [3H, d, *J* 6.9, CH(C*H*$_3$)Ph], 2.09 [3H, d, *J* 7.0, =CH-C*H*$_3$], 4.92-5.09 [1H, m, NC*H*(CH_3)Ph], 6.93-7.02 (2H, m, Ar*H*), 7.12-7.33 (9H, m, Ar*H*, N*H*), 7.67 [1H, q, *J* 7.0, C(3)*H*=]; δ_C (75.5 MHz, $CDCl_3$) 17.1, 22.1 [2 × CH_3, =CH*C*H$_3$ and CH(*C*H$_3$)Ph], 49.6 (CH, N*C*H), 126.2, 126.7, 127.5, 127.7 (CH, aromatic *C*H), 128.9 (C, aromatic *C* or S*C*=), 128.9, 129.8 (CH, aromatic *C*H), 135.3, 143.3 (C, aromatic *C* or S*C*=), 147.8 [CH, *C*(3)H=], 163.71 (C, *C*O); MS *m/z* 297 (M^+, 73%), 282 [8%, $(M\text{-}CH_3)^+$], 149 [47%, $(PhS{=}C{=}CHCH_3)^+$], 120 {43%, $[NHCH(Me)Ph]^+$}, 105 {100%, $[CH(Me)Ph]^+$}, 77 (48, $[C_6H_5]^+$), 43 (92, $[CONH]^+$).

***N,N*-Dimethyl-2-(phenylthio)-2-butenamide 10d**

This was obtained following the procedure for **10c** using **1d**-*Z* (0.40 g, 1.65 mmol), CuI (0.63 g, 3.31 mmol), and methyl lithium (4.2 mL, 1.6 M in ether, 6.61 mmol) in dry ether (50 mL) for 1.75 h at –70 °C. Proton NMR spectroscopic analysis of the crude product mixture indicated a 3.6:1.0 ratio of *Z* to *E* isomers of the adduct with no trace of starting material. Following chromatography,

using 4:1:5 ethyl acetate/dichloromethane/hexane as eluent, an inseparable mixture of *E* and *Z* adducts was recovered as a yellow oil (0.12 g, 34%). While initially a 4:1 ratio of *Z* to *E* isomers was present, isomerisation over three weeks gave a 1:1 ratio of *Z* to *E* when the mixture was stored as a neat oil at room temperature; ν_{max}/cm^{-1} (film) 3344 (NH), 1709 (CO), 1634 (C=C); δ_H (300 MHz, $CDCl_3$) 1.74 [3H, d, *J* 7.1, =CHC*H*$_3$ (*E*)], 1.94 [3H, d, *J* 6.8, =CHC*H*$_3$ (*Z*)], 2.70, 2.87 [6H, 2 × br s, N(C*H*$_3$)$_2$ (*Z*)], 2.81, 2.86 [6H, 2 × s, N(C*H*$_3$)$_2$ (*E*)], 5.95 [1H, q, *J* 7.1, =C*H*CH$_3$ (*E*)], 6.18 [1H, q, *J* 6.8, =C*H*CH$_3$ (*Z*)], 7.18-7.57 (10H, m, Ar*H* for both isomers); δ_C (75.5 MHz, $CDCl_3$) 15.0*, 15.9 [CH_3, =CH*C*H$_3$ (*E*+*Z*)], 34.3, 34.8, 37.6, 38.6 [CH_3, N(*C*H$_3$)$_2$ (*E*+*Z*)], 127.5, 127.9, 128.8, 130.9, 131.5, 132.1, 132.5 [aromatic *C*, *C*(3)H=, =*C*S], 167.5, 168.3* [C, *C*O (*E*+*Z*)], (Some CH and C signals in aromatic region not seen); MS *m/z* 149 [35%, $(PhS{=}C{=}CHCH_3)^+$], 77 [66%, $(C_6H_5)^+$], 72 [78%, $(CONMe_2)^+$], 43 [100%, $(CONH)^+$]. Note: Isomeric ratios were calculated using the integration traces of the β-hydrogen peaks in ^{1}H NMR spectra.

* *Z* isomer

This experiment was repeated on the same scale, with the same conditions, using the *E* isomer of the starting material **1d**-*E*, giving a 3:8 initial ratio of *Z* to *E* adducts, which after chromatography had converted to a 1.1:1.0 ratio (71% yield). Spectroscopic details were identical to those described above.

_N_-Ethyl-2-(phenylthio)-2-butenamide 10e

This was obtained following the procedure for **10c** using **1e** (0.40 g, 1.66 mmol), CuI (0.79 g, 4.15 mmol), and methyl lithium (5.2mL, 1.6 M solution in ether, 8.30 mmol) in dry ether (55 mL) for 2.5 h at –78 °C. The crude product mixture contained a 0.8:1 ratio of starting material **1e** to *Z* adduct **10e**-*Z*, with a trace of **10e**-*E*. Following chromatography using 25:75 ethyl acetate/hexane as eluent, an initial fraction containing starting material (20%) was recovered. A second fraction contained a 1 : 4.5 : 0.4 ratio of starting material **1e** to **10e**-*Z* to **10e**-*E*; δ_H (270 MHz, $CDCl_3$) 6.68 [1H, q, *J* 7.0, C(3)*H*= (*E*)]. The pure product **10e**-*Z* was isolated as an oil (0.12 g, 34%); δ_H (270 MHz, $CDCl_3$) 0.97 (3H, t, *J* 7.6, NCH$_2$C*H*$_3$), 2.04 [3H, d, *J* 7.0, C(4)*H*$_3$], 3.18-3.34 (2H, m, *J* 7.6, NC*H*$_2$CH$_3$), 7.00 (1H, br s, N*H*), 7.12-7.34 (5H, m, Ar*H*), 7.69 [1H, q, *J* 7.0, C(3)*H*=].

_N-i_-Propyl-2-(phenylthio)-2-butenamide 10f

This was obtained following the procedure for **10c** using **1f** (0.40 g, 1.57 mmol), CuI (0.59 g, 3.14 mmol), and methyl lithium (3.9 mL, 1.6 M solution in ether, 6.27 mmol) in dry ether (50 mL) for 2.5 h reaction time at –78 °C. The crude product mixture contained a 1.5:1 ratio of starting

material **1f** to *Z* adduct **10f**-*Z*, and was treated with excess morpholine (~0.2 mL) as before, and following chromatography on silica gel using 20:80 ethyl acetate/hexane as eluent, the pure product **10f**-*Z* was recovered as an oil (0.07 g, 20%); ν_{max}/cm^{-1} (film) 3383 (NH), 1660 (CO), 1612, 1588 (C=C), 1519; δ_H (300 MHz, $CDCl_3$) 0.98 [6H, d, *J* 6.5, CH(C*H*$_3$)$_2$], 2.05 (3H, d, *J* 7.0, =CH-C*H*$_3$), 3.90-4.09 [1H, m, *J* 6.5, C*H*(CH$_3$)$_2$], 6.73 (1H, br d, N*H*), 7.12-7.55 (5H, m, Ar*H*), 7.54 [1H, q, *J* 7.0, C(3)*H*=]; δ_C (75.5 MHz, $CDCl_3$) 15.6 (CH$_3$, =CH*C*H$_3$), 21.3, 21.4 [2 × CH$_3$, CH(*C*H$_3$)$_2$], 40.8 [CH, *C*H(CH$_3$)$_2$], 125.1, 126.0, 128.0 (CH, aromatic *C*H), 133.3, 134.1 (C, aromatic *C*, S*C*=), 145.9 [CH, *C*(3)H=], 162.3 (C, *C*O); MS *m/z* 235 (M^+, 85%), 192 [8%, (M-*i*-Pr)$^+$], 177 [14%, (M-NH-*i*-Pr)$^+$], 149 [58%, (PhS=C=CHCH$_3$)$^+$], 109 [57%, (PhS)$^+$], 43 [100%, (CONH)$^+$]; There was also evidence for the presence of the *E* isomer in trace amounts; δ_H 6.65 [q, *J* 7.0, C(3)*H*=].

_N_-(2-Propenyl)-2-(phenylthio)-2-butenamide 10h

This was obtained following the procedure for **10c** using **1h** (0.40 g, 1.58 mmol), CuI (0.60 g, 3.16 mmol), and methyl lithium (4.0 mL, 1.6 M solution in ether, 6.32 mmol) in dry ether (55 mL) for 2.25 h reaction time, giving a crude mixture containing a 0.3 : 1 : 0.1 ratio of starting material **1h** to **10h**-*Z* to **10h**-*E*. Following chromatography on silica gel using 12:88 ethyl acetate/hexane as eluent, an initial fraction was recovered containing a 0.7 : 1 : 0.05 ratio of starting material **1h** to **10h**-*Z* to **10h**-*E*. The addition product **10h**-*Z* was isolated in a second fraction as a pale yellow oil (0.16 g, 42%); ν_{max}/cm^{-1} (film) 3388 (NH), 1659 (CO), 1612, 1583 (C=C), 1514; δ_H (300 MHz, $CDCl_3$) 2.08 (3H, d, *J* 7.0, =CHC*H*$_3$), 3.82-3.91 (2H, m, NC*H*$_2$CH=CH$_2$), 4.85-5.02 (2H, m, NCH$_2$CH=C*H*$_2$), 5.59-5.78 (1H, m, NCH$_2$C*H*=CH$_2$), 7.04-7.33 (6H, m, Ar*H*, N*H*), 7.75 [1H, q, *J* 7.0, C(3)*H*=]; δ_C (75.5 MHz, $CDCl_3$) 17.1 (CH$_3$, =CH*C*H$_3$), 42.6 (CH$_2$, N*C*H$_2$), 116.3 (CH$_2$, NCH$_2$CH=*C*H$_2$), 126.5, 127.1, 129.7 (CH, aromatic *C*H), 134.1 (CH, CH$_2$*C*H=CH$_2$), 135.2 (C, aromatic *C* or S*C*=), 148.9 [CH, *C*(3)H=], 164.6 (C, *C*O); MS *m/z* 233 (M^+, 7%), 218 [18%, (M-CH$_3$)$^+$], 149 [33%, (PhS=CH=CHCH$_3$)$^+$], 109 [55%, (PhS)$^+$], 77 [57%, (C_6H_5)$^+$], 55 [81%, (NCH$_2$CH=CH$_2$)$^+$], 43 [100%, (CONH)$^+$], 41 [95%, (CH$_2$CH=CH$_2$)$^+$]. This fraction also contained a trace of **10h**-*E*; δ_H 6.73 [1H, q, *J* 7.0, C(3)*H*=].

_N_-*n*-Butyl-2-(phenylthio)-2-butenamide 10i

This was obtained following the procedure for **10c** using **1i** (0.36 g, 1.32 mmol), CuI (0.50 g, 2.64 mmol), and methyl lithium (3.3 mL, 1.6 M solution in ether, 5.29 mmol) in dry ether (50 mL) for 3.5 h reaction time at –50 °C. The crude product contained a 0.75 : 1.0 ratio of starting material **1i**

to adduct **10i**, and was treated with morpholine (~0.2 mL) as outlined previously. Following chromatography on silica gel using 20:80 ethyl acetate/hexane as eluent, the product was recovered as an off-white solid (0.10 g, 29%); ν_{max}/cm^{-1} (KBr) 3338 (NH), 1651 (CO), 1613, 1583 (C=C), 1518; δ_H (300 MHz, $CDCl_3$) 0.78 [3H, t, *J* 7.3, C(4′)H_3], 1.02-1.16 [2H, m, C(3′)H_2], 1.25-1.39 [2H, m, C(2′)H_2], 2.06 (3H, d, *J* 6.9, =CHCH_3), 3.15-3.28 (2H, m, NCH_2), 6.99 (1H, br s, N*H*), 7.12-7.32 (5H, m, Ar*H*), 7.69 [1H, q, *J* 6.9, C(3)*H*=]; δ_C (75.5 MHz, $CDCl_3$) 13.7 [CH_3, *C*(4′)H_3], 16.7 (CH_3, =CH*C*H_3), 19.8 [CH_2, *C*(3′)H_2], 31.4 [CH_2, C(2′)H_2], 39.6 (CH_2, N*C*H_2), 126.0, 126.7 (CH, aromatic *C*H), 127.1 (C, aromatic *C* or S*C*=), 129.3 (CH, aromatic *C*H), 134.1 (C, aromatic *C* or =*C*S), 147.6 [CH, *C*(3)H=], 164.1 (C, *C*O); MS *m/z* 249 (M^+, 5%), 234 [15%, $(M\text{-}CH_3)^+$], 149 [12%, $(PhS{=}C{=}CHCH_3)^+$], 109 [26%, $(PhS)^+$], 72 [74%, $(NHC_4H_9)^+$], 57 [87%, $(C_4H_9)^+$], 43 [100%, $(CONH)^+$]. There was also a trace (~ 5%) of the *E* adduct present; δ_H 6.69 [1H, q, *J* 6.9, C(3)*H*=].

_N_-Methyl-2-(phenylthio)-2-butenamide 10j

This was obtained following the procedure for **10c** using **1j** (0.30 g, 1.32 mmol), CuI (0.50 g, 2.64 mmol), and methyl lithium (3.3 mL, 1.6 M solution in ether, 5.29 mmol) in dry ether (50 mL) for 3.5 h reaction time at –50 °C. The crude product contained a 1:2.4 ratio of starting material **1j** to adduct **10j**, and was treated with morpholine (~0.2 mL) as outlined previously. Following chromatography on silica gel using 15:85 ethyl acetate/hexane as eluent, the product **10j** was recovered as a white solid (0.08 g, 29%); mp 55−56 °C; (Found C, 63.74; H, 6.69; N, 6.72; S, 15.02; $C_{11}H_{13}NOS$ requires C, 63.74; H, 6.32; N, 6.76; S, 15.45%); ν_{max}/cm^{-1} (film) 3336 (NH), 1651 (CO), 1612, 1583 (C=C), 1520; δ_H (300 MHz, $CDCl_3$) 2.05 (3H, d, *J* 7.0, =CHCH_3), 2.79 (3H, d, *J* 6.0, NCH_3), 6.98 (1H, br s, N*H*), 7.07-7.30 (5H, m, Ar*H*), 7.75 [1H, q, *J* 7.0, C(3)*H*=]; δ_C (75.5 MHz, $CDCl_3$) 16.7 (CH_3, =CH*C*H_3), 26.9 (CH_3, N*C*H_3), 125.9, 126.4 (CH, aromatic *C*H), 126.5 (C, aromatic *C* or S*C*=), 129.3 (CH, aromatic CH), 134.9 (C, aromatic *C* or S*C*=), 148.3 [CH, *C*(3)H=], 165.0 (C, *C*O); MS *m/z* 208 (M^++1, 82%), 149 [30%, $(PhS{=}C{=}CHCH_3)^+$], 134 [29%, $(PhS{=}C{=}CH)^+$], 109 [31%, $(PhS)^+$], 98 [26%, $(M\text{-}PhS)^+$], 77 [44%, $(C_6H_5)^+$], 58 [84%, $(CONHCH_3)^+$], 43 [100%, $(CONH)^+$]. There was also a trace of the *E* isomer present; δ_H 6.70 [1H, q, *J* 7.0, C(3)*H*=].

2-(Phenylthio)-2-butenamide 10k

This was obtained following, using **1k** (0.20 g, 0.95 mmol), CuI (0.36 g, 1.89 mmol) and methyl lithium (2.7 mL, 1.4 M in ether, 3.79 mmol) in dry ether (35 mL) for 2 h at –57 °C. The crude

product mixture, containing a 0.7:1 ratio of starting material to adduct, was reacted with morpholine (~0.2 mL) as before to remove the excess starting material, giving after chromatography on silica gel using 4:1:5 ethyl acetate/dichloromethane/hexane as eluent, the pure product **10k** as a white solid (0.07 g, 39%); ν_{max}/cm^{-1} (KBr) 3414 (NH), 1652 (CO), 1605 (C=C); δ_H (300 MHz, $CDCl_3$) 2.08 (3H, d, *J* 7.0, =CHC*H*$_3$), 6.03, 6.84 (2H, 2 × br s, N*H*$_2$), 7.12-7.30 (5H, m, Ar*H*), 7.73 [1H, q, *J* 7.0, C(3)*H*=]; δ_C (75.5 MHz, $CDCl_3$) 17.2 (CH_3, =CH*C*H$_3$), 126.5 (CH, aromatic *C*H), 126.8 (C, aromatic *C* or S*C*=), 127.1, 129.7 (CH, aromatic *C*H), 135.2 (C, aromatic *C* or S*C*=), 149.9 [CH, *C*(3)H=], 167.2 (C, *C*O); MS *m/z* 193 (M^+, 3%), 149 [23%, $(PhS=C=CHCH_3)^+$], 43 [100%, $(CONH)^+$]. There was no evidence for the presence of the *E* isomer.

Addition of Ph_2CuLi

N-(4-Methylphenyl)-3-phenylpropynamide 11a[24]

This was obtained following the method described for **11c**, using **1a** (0.50 g, 1.65 mmol), CuI (0.63 g, 3.30 mmol) and phenyl lithium (3.7 mL, 1.8 M solution in ether, 6.60 mmol) in ether (50 mL) at −78 °C for 2.5 h. Following column chromatography on silica gel using 20:80 ethyl acetate/hexane as eluent, **11a** was isolated as a solid (0.12g, 31%); mp 139−141 °C (lit.[24] 140-141 °C); ν_{max}/cm^{-1} (film) 2214(C≡C), 1636(CO); δ_H (300 MHz) 2.33 (3H, s, ArC*H*$_3$), 7.08-7.62 (9H, m, Ar*H*), 7.69 (1H, br s, N*H*); δ_C (75 MHz) 20.9 (CH_3, Ar*C*H$_3$), 83.6, 85.6 (C, *C*≡*C*), 120.0 (C, aromatic *C*), 120.1, 128.5, 129.6, 130.2, 132.6 (CH, aromatic *C*H), 134.6, 134.9 (C, aromatic *C*), 151.1 (C, *C*O).

***N-i*-Propyl-3-phenylpropynamide 11f**

This was obtained following the method described for **11a** using **1f** (0.25 g, 0.96 mmol), CuI (0.37 g, 1.93 mmol) and phenyl lithium (2.2 mL, 1.8 M solution in ether, 3.85 mmol) in ether (40 mL) for 2 h at −78 °C. After chromatography on silica gel using 12:88 ethyl acetate/hexane as eluent, the initial fractions contained a mixture of **1f** and aromatic side products. In the third fraction the pure alkynamide **11f** was recovered as a white solid (0.14 g, 77%); mp 68−70 °C; (Found C, 76.70; H, 6.91; N, 7.52. $C_{12}H_{13}NO$ requires C, 76.98; H, 6.99; N, 7.48%); ν_{max}/cm^{-1} (KBr) 3248 (NH), 2221 (C≡C), 1625 (C=O); δ_H (300 MHz, $CDCl_3$) 1.22 [6H, d, *J* 6.5, NCH(C*H*$_3$)$_2$], 4.10-4.27 [1H, m, *J* 6.5, NC*H*(CH$_3$)$_2$], 5.89 (1H, br s, N*H*), 7.25-7.59 (5H, m, Ar*H*); δ_C (67.8 MHz, $CDCl_3$) 22.6 [CH_3, CH(*C*H$_3$)$_2$], 42.0 [CH, *C*H(CH$_3$)$_2$], 83.4, 84.0 (C, *C*≡*C*), 120.4 (C, aromatic *C*), 128.4,

129.8, 132.3 (CH, aromatic *C*H), 152.5 (C, *C*O); MS *m/z* 187 (M^+, 18%), 172 [17%, $(M\text{-}CH_3)^+$], 129 [100%, $(PhC{\equiv}C\text{-}C{=}O)^+$], 102 (13%, Ph-C≡CH), 58 [11%, $(NH\text{-}i\text{-}Pr)^+$].

Nitrogen Nucleophiles

Addition of primary and secondary amines

N-(4-Benzyl)-3-N′,N′-dimethylamino-2-(benzylthio)propenamide 14v

This was prepared following the procedure described for propenamide **14a** using dimethylamine (5.6 M in ethanol, 4 mL, 22.6 mmol) and **1v** (0.3 g, 0.94 mmol). The reaction was complete by TLC analysis after 15 min to give the crude product **14v** as a yellow oil (0.239 g, 78%). ^{1}H NMR spectroscopic analysis showed that no further purification was required; ν_{max}/cm^{-1} (film) 3382 (NH), 1637 (CO amide); δ_H (400 MHz, $CDCl_3$) 2.92 [6H, s, $N(CH_3)_2$], 3.53 (2H, s, CH_2S), 4.43 (2H, d, *J* 5.9, $NHCH_2$), 7.08-7.38 (10H, m, Ar*H*), 7.51 (1H, br t, *J* 5.3, N*H*), 7.97 [1H, s, C(3)*H*]; δ_C (75.5 MHz, $CDCl_3$) 42.6 (CH_2, SCH_2 or $NHCH_2$), 43.0 (CH_3, br, CH_3N), 44.1 (CH_2, SCH_2 or $NHCH_2$), 85.7 [C, *C*(2)S], 127.0, 127.6, 128.4, 128.5, 128.9 (5 × CH, aromatic *C*H), 138.1, 139.6 (2 × C, aromatic *C*), 152.8 [CH, *C*(3)H], 169.4 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{19}H_{23}N_2OS$ ($M+H^+$) 327.1531. Found 327.1527 ($M+H^+$); m/z (ESI^+) 327.2 ($M+H^+$).

N-(4-Methylphenyl)-3-N′,N′-diethylamino-2-(phenylthio)propenamide 15a

This was prepared following the procedure described for propenamide **14a** using diethylamine (8 mL, 4.1 M in ethanol, 33 mmol), and **1a** (0.30 g, 0.99 mmol). The reaction was complete by TLC analysis after 10 min to give the crude product **15a** (0.31 g, 92%). Recrystallisation from ether gave **15a** (0.25 g, 73%) as a white, crystalline solid; mp 105−106 °C; (Found C, 70.74; H, 7.03; N, 8.35; S, 9.47. $C_{20}H_{24}N_2OS$ requires C, 70.55; H, 7.11; N, 8.23; S, 9.42%); ν_{max}/cm^{-1} (KBr) 3346 (br NH), 1652, 1583 (CO α,β-unsaturated amide); δ_H (270 MHz, $CDCl_3$) 1.17 (6H, t, *J* 7, CH_3CH_2N), 2.26 (3H, s, $ArCH_3$), 3.35-3.65 (4H, br m, NCH_2), 7.04-7.39 (9H, m, Ar*H*), 8.35 [1H, s, C(3)*H*=], 8.88 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) CH_2N broadened into the baseline at δ_C 42-51, 14.6 (CH_3, CH_3CH_2N), 20.8 (CH_3, $ArCH_3$), 82.0 (S*C*=), 119.90, 119.92, 124.8, 125.2, 129.2 (CH, aromatic *C*H), 132.5, 136.7,

139.1 (aromatic *C*), 152.2 [CH, *C*(3)H=], 167.3 (*C*O); MS *m/z* 340 (M^+, 45 %), 234 (100%), 206 (31%), 110 (43%).

_N_-(4-Benzyl)-3-_N′_,_N′_-diethylamino-2-(benzylthio)propenamide 15v

This was prepared following the procedure described for propenamide **14a** using diethylamine (4.1 M in ethanol, 4 mL, 16.5 mmol) and **1v** (0.15 g, 0.47 mmol). The reaction was complete by TLC analysis after 15 min to give the product **15v** as a yellow oil (0.16 g, 95 %). ^{1}H NMR spectroscopic analysis showed that no further purification was required; ν_{max}/cm^{-1} (film) 3386 (NH), 1633 (CO amide); δ_H (400 MHz, $CDCl_3$) 1.05 [6H, t, *J* 7.1 N(CH_2CH_3)$_2$], 3.24-3.39 [4H, br m, N(CH_2CH_3)$_2$], 3.56 (2H, s, SCH_2), 4.41 (2H, d, *J* 5.9, NHCH_2), 7.07-7.13 (2H, m, Ar*H*), 7.15-7.35 (8H, m, Ar*H*), 7.50 (1H, br t, *J* 5.6, N*H*), 8.00 [1H, s, C(3)*H*]; δ_C (75.5 MHz, $CDCl_3$) CH_2N broadened into the baseline at δ_C 42-51, 14.0 [CH_3, 2 × N(CH_2CH_3)$_2$], 42.2 (CH_2, SCH_2 or NHCH_2), 44.1 (CH_2, SCH_2 or NHCH_2), 84.8 [C, *C*(2)S], 127.0, 127.6, 128.46, 128.53, 128.9 (5 × CH, aromatic *C*H), 137.9, 139.6 (2 × C, aromatic *C*), 150.7 [CH, *C*(3)H], 169.5 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{21}H_{27}N_2OS$ ($M+H^+$) 355.1844. Found 355.1834 ($M+H^+$); m/z (ESI^+) 355.2 ($M+H^+$).

***N*-(4-Methylphenyl)-3-diisopropylamino-2-(phenylthio)propenamide 16a**

β-Chloroacrylamide **1a** (100 mg, 0.33 mmol) was added to neat DIPA (3 mL) with stirring. After stirring for 1 h the reaction was complete by TLC analysis and CH_2Cl_2 (10 mL) and water (10 mL) were added. The phases were separated and the aqueous layer was washed with CH_2Cl_2 (2 × 5 mL). The combined organic layers were washed with aqueous saturated aqueous ammonium chloride (2 × 10 mL), brine (2 × 10 mL), dried and evaporated. The ^{1}H NMR spectrum of the crude product mixture showed that it was **16a**; δ_H (270 MHz, $CDCl_3$) 1.22-1.28 {6H, br m, [(CH_3)$_2$CH]$_A$N}, 1.48 {6H, d, *J* 7, [(CH_3)$_2$CH]$_B$N}, 2.26 (3H, s, ArCH_3), 3.31-3.35 (1H, sept, *J* 7, NCH_B), 3.50-3.72 (1H, br m, NCH_A), 7.03-7.40 (9H, m, Ar*H*), 8.52 [1H, s, C(3)*H*=], 8.90 (1H, br s, N*H*).

***N*-(4-Methylphenyl)-3-morpholino-2-(phenylthio)propenamide 17a**

Morpholine (72 μl, 0.83 mmol) was added to a solution of **1a** (100 mg, 0.33 mmol) in CH_2Cl_2 (3 mL). The reaction was complete by TLC analysis after 5 min at room temperature and aqueous saturated aqueous ammonium chloride (10 mL) was added. The phases were separated and the aqueous layer was washed with CH_2Cl_2 (2 × 5 mL). The combined organic

layers were washed with aqueous sodium bicarbonate (2 × 10 mL), brine (2 × 10 mL), dried and evaporated to give a white, crystalline solid (95 mg). Recrystallisation from ethyl acetate-hexane (1:9) gave β-morpholinopropenamide **17a** (78 mg, 67%) as a white, crystalline solid; mp 125−127 °C; (Found C, 67.61; H, 6.34; N, 7.83; S, 8.38. $C_{20}H_{22}N_2O_2S$ requires C, 67.77; H, 6.26; N, 7.90; S, 9.05%); ν_{max}/cm^{-1} (KBr) 3342 (br NH), 1647, 1576 (CO amide); δ_H (270 MHz, $CDCl_3$) 2.77 (3H, s, ArCH_3), 3.59-3.71 [4H, m, C(3′)H_2 and C(5′)H_2], 3.76-3.84 [4H, m, C(2′)H_2 and C(6′)H_2], 7.05-7.42 (9H, m, Ar*H*), 8.26 [1H, s, C(3)*H*=], 8.85 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 20.7 (Ar*C*H_3), 50.8 (broad, N*C*H_2), 66.8 (O*C*H_2), 83.9 (S*C*=), 119.8, 125.0, 125.5, 129.2, 129.3 (aromatic *C*H), 132.8, 136.3, 137.6 (aromatic *C*), 152.1 [*C*(3)H=], 166.7 (*C*O); MS *m/z* 354 (M^+, 3%), 268 [3%, M^+-N$(CH_2CH_2)_2$O], 248 (4%, M^+-NHTol).

***N*,*N*-Dimethyl-3-morpholino-2-(phenylthio)propenamide 17d**

Morpholine (135 μl, 1.55 mmol) was added to a stirred solution of *N,N*-dimethyl-*E*-3-chloro-2-(phenylthio)propenamide *E*-**1d** (150 mg, 0.62 mmol) in CH_2Cl_2 (3 mL) at room temperature. After 4 h the reaction was incomplete by TLC analysis and a further 2 equivalents of morpholine (100 μl, 1.15 mmol) were added. After 23 h the reaction was complete by TLC and water (10 mL) and CH_2Cl_2 (10 mL) were added. The organic phase was washed with water (2 × 10 mL) and brine (10 mL), dried and evaporated to give **17d**; δ_H (60 MHz, $CDCl_3$) 2.86 (6H, s, NCH_3), 2.90-3.78 [8H, m, N(CH_2CH_2)$_2$O], 6.51 [1H, s, C(3)*H*=], 6.95-7.50 (5H, m, Ar*H*).

***N*-*i*-Propyl-3-morpholino-2-(phenylthio)propenamide 17f**

This was prepared following the procedure described for β-morpholinopropenamide **14a** using **1f** (100 mg, 0.39 mmol), morpholine (85 μl, 0.98 mmol) and CH_2Cl_2 (2 mL) for a reaction time of 30 min to give the crude propenamide **17c**. Trituration with ether-hexane (1:99) gave **17f** (105 mg, 88%) as a white, crystalline solid; mp 95−97 °C; (Found C, 62.54; H, 7.00; N, 9.30; S, 10.59. $C_{16}H_{22}N_2O_2S$ requires C, 62.71; H, 7.24; N, 9.14; S, 10.46%); ν_{max}/cm^{-1} (film) 3386 (br NH), 1629, 1578 (CO α,β-unsaturated amide); δ_H (270 MHz, $CDCl_3$) 1.07 [6H, d, *J* 7, (CH_3)$_2$CHN], 3.56-3.63, 3.70-3.82 [2 × 4H, 2 × m, N(CH_2CH_2)$_2$O], 4.00-4.13 (1H, sym m, *J* 7, 8, NC*H*), 6.81 (1H, br d, *J* 7, N*H*), 7.10-7.30 (5H, m, Ar*H*), 8.16 [1H, s, C(3)*H*=]; δ_C (67.8 MHz, $CDCl_3$) 22.4 [(*C*H_3)$_2$CHN], 41.7 (N*C*H), 50.6 (*C*H_2N), 66.8

(*C*HO), 84.1 (S*C*=), 125.0, 125.2, 129.1 (aromatic *C*H), 138.0 (aromatic *C*), 151.4 [*C*(3)H=], 167.7 (*C*O); MS *m/z* 306 (M^+, 5%), 248 [1%, M^+-NHCH$(CH_3)_2$], 99 (95%), 56 (100%).

(1′S)-*N*-(1-Phenylethyl)-*Z*-3-morpholino-2-(phenylthio)pentenamide 17l-*Z*, (1′S)-*N*-(1-phenylethyl)-*Z*-3-morpholino-2-(phenylthio)pentenamide 17l-*E*

Morpholine (19 µl, 0.22 mmol) was added to a stirred solution of **1l-*E*** (30 mg, 0.09 mmol) in CH_2Cl_2 (1 mL). The reaction was incomplete by TLC analysis after 96 h at room temperature. Aqueous saturated ammonium chloride (10 mL) was added, the phases were separated and the aqueous layer was washed with CH_2Cl_2 (2 × 5 mL). The combined organic layers were washed with aqueous sodium bicarbonate (2 × 10 mL), brine (2 × 10 mL), dried and evaporated to give a mixture of three compounds tentatively assigned as *E* and *Z* isomers of **17l** (in a ratio of 1.2:1) and **1l-*E*** as a white solid (65 mg).

Also, morpholine (32 µl, 0.36 mmol) was added to a stirred solution of **1l-*Z*** (50 mg, 0.15 mmol) in CH_2Cl_2 (2 mL). The reaction was complete by TLC analysis after 22 h at room temperature. Aqueous saturated ammonium chloride (10 mL) was added, the phases were separated and the aqueous layer was washed with CH_2Cl_2 (2 × 5 mL). The combined organic layers were washed with aqueous sodium bicarbonate (2 × 10 mL), brine (2 × 10 mL), dried and evaporated to give a mixture of two compounds tentatively assigned as *E* and *Z* isomers of **17l** in a ratio of 1:1.3 as a white solid (67 mg). **17l-*Z***; δ_H (270 MHz, $CDCl_3$) 1.12 [3H, t, *J* 5, C(5)H_3], 1.13 [3H, d, *J* 6, C(2′)H_3], 2.74 [2H, q, *J* 5, C(4)H_2], 3.40-3.43, 3.74-3.79 {8H, m, N[(CH_2)$_2$]$_2$ O}, 4.90-5.20 [1H, m, C(1′)*H*], 6.91-7.45 (11H, m, Ar*H*, N*H*); and **17l-*E*** δ_H (270 MHz, $CDCl_3$) 1.14 [3H, t, *J* 5, C(5)H_3], 1.40 [3H, d *J* 6, C(2′)H_3], 2.68 [2H, q, *J* 5, C(4)H_2], 2.85-2.89, 3.66-3.70 {8H, m, N[(CH_2)$_2$]$_2$O}, 4.90-5.2 [1H, m, C(1′)*H*], 6.91-7.45 (11H, m, Ar*H*, N*H*).

N*-(4-Methylphenyl)-*Z*-3-morpholino-2-(phenylthio)pentenamide 17m-*Z*, *N*-(4-methylphenyl)-*E*-3-morpholino-2-(phenylthio)pentenamide 17m-*E

Morpholine (66 µl, 0.75 mmol) was added to a stirred solution of *Z*-**1m** (100 mg, 0.30 mmol) in CH_2Cl_2 (3 mL). The reaction was incomplete by TLC analysis after 2 h at room temperature, therefore further morpholine (66 µl, 0.75 mmol) was added and the reaction mixture was stirred at room temperature for 16 h, after which TLC analysis showed complete reaction. Aqueous saturated aqueous ammonium chloride (10 mL) was added, the phases

were separated and the aqueous layer was washed with CH_2Cl_2 (2 × 5 mL). The combined organic layers were washed with aqueous sodium bicarbonate (2 × 10 mL), brine (2 × 10 mL), dried and evaporated to give a mixture of two compounds tentatively assigned as *E* and *Z* isomers of **17m** in a ratio of 4:1, as a colourless oil (98 mg). Some signals could be distinguished for the major isomer (assigned *E*) at δ_H (270 MHz, $CDCl_3$) 2.29 (s, ArC*H*$_3$) 2.65 [q, *J* 7, C(4)*H*$_2$], 2.85-2.89, 3.66-3.70 [N(*C*H$_2$*C*H$_2$)$_2$O], 8.69 (1H, br s, N*H*), and for the minor isomer (assigned *Z*) at δ_H 2.25 (s, ArC*H*$_3$), 2.79 [q, *J* 7, C(4)*H*$_2$], 3.40-3.43, 3.74-3.79 [N(C*H*$_2$C*H*$_2$)$_2$O], 8.54 (1H, br s, N*H*). Other signals were observed at δ_H (270 MHz, $CDCl_3$) 1.13 [3H, d, *J* 7, C(5)*H*$_3$], 7.01-7.31 (9H, m, Ar*H*).

_N,N_-Diphenyl-_Z_-3-morpholino-2-(phenylthio)propenamide 17n-_Z_ and _N,N_-Diphenyl-_E_-3-morpholino-2-(phenylthio)propenamide 17n-_E_

These were prepared following the procedure described for β-morpholinopropenamide **14a** using *Z*-**1n** (63 mg, 0.17 mmol), morpholine (36 μl, 0.4 mmol) and CH_2Cl_2 (2 mL) with a reaction time of 3 h. Purification by chromatography using ethyl acetate-hexane (50:50) as eluent gave **17n-***Z* (62 mg, 88 %) as a white, crystalline solid; mp 156−158 °C; (Found C, 72.03; H, 5.96; N, 6.58; S, 7.24. $C_{25}H_{24}N_2O_2S$ requires C, 72.09; H, 5.81; N, 6.73; S, 7.70%); ν_{max}/cm^{-1} (film) 1633, 1587 (CO α,β-unsaturated amide); δ_H (270 MHz, $CDCl_3$) 3.50-3.58, 3.63-3.72 [2 × 4H, 2 × m, N(C*H*$_2$C*H*$_2$)$_2$O], 6.85-7.29 (15H, m, Ar*H*), 7.70 [1H, s, C(3)*H*=]; δ_C (67.8 MHz, $CDCl_3$) 50.7 (*C*H$_2$N), 66.8 (*C*H$_2$O), 89.9 (S*C*=), 124.5, 125.3, 126.1, 126.8, 128.9, 129.3 (aromatic *C*H), 126.4, 140.1, 145.3 (aromatic *C*), 153.7 [*C*(3)H=], 174.1 (*C*O); MS *m/z* 416 (M^+, 1 %), 331 [3, M^+-N(CH$_2$CH$_2$)$_2$O +H], Signals for the isomer tentatively assigned as the *E* isomer **17f-***E* (*ca.* 8%) could be seen in the ^{1}H NMR spectrum at δ_H (270 MHz, $CDCl_3$) 3.39-3.45, 3.76-3.84 [2 × 4H, 2 × m, N(C*H*$_2$C*H*$_2$)$_2$O], 6.72 [C(3)*H*=]; δ_C (67.8 MHz, $CDCl_3$) 53.5 (*C*H$_2$N), 66.4 (*C*H$_2$O), 91.5 (S*C*=), 169.5 (*C*O).

_N_-(4-Fluorophenyl)-_Z_-3-morpholino-2-(benzylthio)propenamide 17o

Morpholine (0.13 mL, 1.45 mmol) was added to a solution of **1o** (0.19 g, 0.58 mmol) in CH_2Cl_2 (4 mL). The reaction progress was monitored by TLC, which indicated that the reaction was complete after 10 min. Aqueous saturated ammonium chloride (10 mL) was added to the reaction mixture and the phases were then separated. The aqueous layer was extracted with dichloromethane (2 × 5 mL) and the combined organic layers were then washed with aqueous sodium bicarbonate (2 × 10 mL), brine (2 × 10 mL), dried, filtered and

the solvent was evaporated under reduced pressure to give **17o** (0.15 g, 71%) as a white solid which required no further purification, mp 98−100 °C; ν_{max}/cm^{-1} (KBr) 3338 (NH), 2961 (CH), 1651 (CO), 1579 (NH bend), 1509; δ_H (300 MHz, $CDCl_3$) 3.48-3.62 [8H, m, N(CH_2CH_2)$_2$O], 3.65 (2H, s, SCH_2), 6.94-7.02 (2H, overlapping m, Ar*H*), 7.15-7.33 (5H, m, Ar*H*), 7.38-7.47 (2H, m, Ar*H*), 7.98 [1H, s, C(3)*H*=], 9.04 (1H, br s, N*H*); δ_c (75.5 MHz, $CDCl_3$) 42.2 [CH_2, O*C*(3′)H_2 & O*C*(5′)H_2], 50.9 [CH_2, broad signal, N*C*(2′)H_2 & N*C*(6′)H_2], 66.9 (CH_2, S*C*H_2), 86.6 [C, *C*(2)S], 115.7 [CH, d, $^2J_{CF}$ 22, aromatic *C*(3′)H], 121.6 [CH, d, $^3J_{CF}$ 8, aromatic C(2′)H], 127.8, 129.0, 129.3 (3 × CH, 3 × aromatic *C*H), 135.4, 138.1 (2 × C, 2 × aromatic *C*), 152.1 [CH, *C*(3)H=], 159.2 [C, d, $^1J_{CF}$ 242, aromatic *C*(4′)], 167.5 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{20}H_{22}N_2O_2SF$ $[M+H]^+$ 373.1386. Found 373.1388; *m/z* (ES+) 373.2 {[($C_{20}H_{21}N_2O_2SF$)+H^+], 100%}.

***N*-*n*-Butyl-*Z*-3-morpholino-2-(benzylthio)propenamide 17p**

The title compound was prepared as described above for **14a** using **1p** (0.19 g, 0.7 mmol) in dichloromethane (5 mL) and morpholine (0.15 mL, 1.7 mmol). TLC analysis showed the reaction to be complete after 10 min and following the work-up, **17p** (0.17 g, 75%) was obtained as a pale yellow oil which required no further purification; ν_{max}/cm^{-1} (KBr) 3387 (NH), 3027 (CH), 2958 (CH), 1640 (CO), 1575 (NH bend), 1505; δ_H (300 MHz, $CDCl_3$) 0.93 [3H, t, *J* 7.2, C(4′)H_3], 1.29-1.53 [4H, m, C(3′)H_2 & C(2′)H_2], 3.25 (2H, q, *J* 6.6, CH_2NH), 3.42-3.52 [8H, m, N(CH_2CH_2)$_2$O], 3.57 (2H, s, SCH_2), 7.12-7.34 (6H, m, Ar*H* & N*H*), 7.88 [1H, s, C(3)*H*=]; δ_c (75.5 MHz, $CDCl_3$) 13.9 [CH_3, *C*(4′)H_3], 20.2 [CH_2, *C*(3′)H_2], 31.4 [CH_2, *C*(2′)H_2], 39.7 (CH_2, *C*H_2NH), 41.4 (CH_2, S*C*H_2), 50.3 [CH_2, br, N*C*(2″)H_2 & N*C*(6″)H_2], 66.5 [CH_2, O*C*(3″)H_2 & O*C*(5″)H_2], 86.6 [C, *C*(2)S], 127.2, 128.5, 128.9 (3 × CH, 3 × aromatic *C*H), 138.0 (C, aromatic *C*), 150.9 [CH, *C*(3)H=], 168.6 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{18}H_{27}N_2O_2S$ $[M+H]^+$ 335.1793. Found 335.1793; *m/z* (ES+) 335.1 {[($C_{18}H_{26}N_2O_2S$)+H^+], 100%}.

***N*-(4-Methylphenyl)-*Z*-3-morpholino-2-(benzylthio)propenamide 17q**

This was synthesised according to the procedure outlined for **14a** using **1q** (0.20 g, 0.6 mmol) in dichloromethane (10 mL) and morpholine (0.13 mL, 1.5 mmol). The reaction was observed to be complete after 30 min by TLC analysis and following the work-up, **17q** was obtained as a brown oil. This was then purified by column chromatography on silica gel using hexane-ethyl acetate as eluent (gradient elution 20-40% ethyl acetate) to give the pure adduct

17q (0.19 g, 87%) as a white solid, mp 115−116 °C; (Found C, 68.06; H, 6.50; N, 7.49; S, 8.85. $C_{21}H_{24}N_2O_2S$ requires C, 68.45; H, 6.56; N, 7.60; S, 8.70%); ν_{max}/cm^{-1} (film) 3317 (NH), 2918 (CH), 1648 (CO), 1578, 1517 (NH bend), 1399 (CN stretch); δ_H (300 MHz, $CDCl_3$) 2.31 (3H, s, ArC*H*$_3$), 3.43-3.59 [8H, m, N(C*H*$_2$C*H*$_2$)$_2$O], 3.64 (2H, s, SC*H*$_2$), 7.11 (2H, d, *J* 8.4, Ar*H*), 7.18-7.34 (5H, m, Ar*H*), 7.40 (2H, d, *J* 8.4, Ar*H*), 7.97 [1H, s, C(3)*H*=], 9.07 (1H, br s, N*H*); δ_c (75.5 MHz, $CDCl_3$) 21.2 (CH_3, Ar*C*H$_3$), 42.1 (CH_2, S*C*H$_2$), 50.8 [CH_2, broad signal, N*C*(2′)H$_2$ & N*C*(6′)H$_2$], 66.9 [CH_2, O*C*(3′)H$_2$ & O*C*(5′)H$_2$], 86.9 [C, *C*(2)S], 120.0, 127.7, 129.0, 129.3, 129.7 (5 × CH, 5 × aromatic *C*H), 133.1, 136.9, 138.1 (3 × C, 3 × aromatic *C*), 152.0 [CH, *C*(3)H=], 167.4 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{21}H_{25}N_2O_2S$ $[M+H]^+$ 369.1637. Found 369.1647; *m/z* (ES+) 369.3 {[($C_{21}H_{24}N_2O_2S$)+H^+], 100%}.

N*-(4-Methylphenyl)-*Z*-3-diisopropylamino-2-(benzenesulfinyl)propenamide 19a-*Z* and *N*-(4-Methylphenyl)-*E*-3-diisopropylamino-2-(benzenesulfinyl)propenamide 19a-*E

This was prepared using the procedure described for **14a** using **18a** (0.30 g, 0.94 mmol), DIPA (0.32 mL, 2.35 mmol) and CH_2Cl_2 (9 mL). The crude product was purified on silica gel using hexane:ethyl acetate (40:60) as eluent to yield **19a** as an inseparable mixture of *Z* and *E* isomers in the ratio 1.7:1 (0.31 g, 87%); mp 49−52 °C; (Found C, 68.80; H, 7.46; N, 7.62; S, 8.29. $C_{22}H_{28}N_2O_2S$ requires C, 68.72; H, 7.34; N, 7.29; S, 8.54%); ν_{max}/cm^{-1} (KBr) 1659 (CO), 1513 (NH bend), 1005; δ_H (300 MHz, $CDCl_3$) 1.06-1.51 [12H, br m, (C*H*$_3$)$_2$CH-*Z* and (C*H*$_3$)$_2$CH-*E*], 2.28 (1.1H, s, ArC*H*$_3$-*E*), 2.33 (1.9H, s, ArC*H*$_3$-*Z*), 3.19-3.31 [0.38H, s, one of (CH$_3$)$_2$C*H*-*E*], 3.54-3.72 [0.38H, s, one of (CH$_3$)$_2$C*H*-*E*], 3.73-4.61 [1.24H, br s, 2 × (CH$_3$)$_2$C*H*-*Z*], 6.91-7.71 [9.4H, m, Ar*H* and =C(3)*H*N-*E*], 8.16 [0.6H, s, =C(3)*H*N-*Z*], 9.21 (0.4H, br s, N*H*-*E*), 9.61 (0.6H, br s, N*H*-*Z*).

19a-*Z* δ_c (75.5 MHz, $CDCl_3$) 19.6 (CH_3, Ar*C*H$_3$), 21.2 [CH_3, (*C*H$_3$)$_2$CH], 47.3 [CH, (CH$_3$)$_2$*C*H], 97.0 [C, *C*(2)], 120.7, 124.8, 129.5, 129.8, 130.3 (CH, aromatic *C*H), 132.7 (C, aromatic *C*), 149.4 [CH, =*C*(3)HN], 166.1 (C, *C*O);

19a-*E* δ_c (75.5 MHz, $CDCl_3$) 19.6 (CH_3, Ar*C*H$_3$), 21.2 [CH_3, (*C*H$_3$)$_2$CH], 48.2 [CH, (CH$_3$)$_2$*C*H], 103.5 [C, *C*(2)], 121.1, 125.4, 129.5, 129.7, 130.2 (CH, aromatic *C*H), 133.8, 144.1 (C, aromatic *C*), 147.4 [CH, =*C*(3)HN], 163.3 (C, *C*O); MS *m/z* 383 (M^+ – 1, 11%).

N*-(4-Methylphenyl)-*Z*-3-diethylamino-2-(phenylsulfinyl)propenamide 20a-*Z* and *N*-(4-Methylphenyl)-*E*-3-diethylamino-2-(phenylsulfinyl)propenamide 20a-*E

This was prepared using the procedure described for **14a** using **18a** (0.2 g, 0.94 mmol) and diethylamine (4.1 M in ethanol, 3 mL, 12.4 mmol). The crude product contained a 1.8:1 mixture of the *Z* and *E* isomers of **20a**. As this compound decomposed to a black complex mixture of unidentified compounds within 1 h of its preparation, purification and full characterisation was not possible; ν_{max}/cm^{-1} (film) 3472 (NH), 1661 (CO amide), 1078 (SO); **20a-*Z*:** δ_H (400 MHz, $CDCl_3$) 1.31 (6H, t, *J* 7.2, C*H*$_3$CH$_2$N), 2.22 (3H, s, ArC*H*$_3$), 3.38-3.59 (4H, br m, NC*H*$_2$), 6.91-7.65 (9H, m, Ar*H*), 7.98 [1H, s, C(3)*H*], 9.68 (1H, s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 13.7 (CH_3, *C*H$_3$CH$_2$N), 20.79 (CH_3, Ar*C*H$_3$), 48.9 (CH_2, br, *C*H$_2$N), 97.1 [C, *C*(2)S], 120.3, 124.7, 129.1, 129.92 (4 × CH, aromatic *C*H), 132.8, 136.1, 144.7 (3 × C, aromatic *C*), 151.6 [CH, *C*(3)H], 165.5 (C, *C*O).

20a-*E*: δ_H (400 MHz, $CDCl_3$) 1.20 (6H, t, *J* 7.2, C*H*$_3$CH$_2$N), 2.22 (3H, s, ArC*H*$_3$), 3.61-3.81 (4H, br m, NC*H*$_2$) , 6.91-7.65 [10H, m, Ar*H* and C(3)*H*], 9.21 (1H, s, N*H*); δ_C (75.5 MHz) 13.7 (CH_3, *C*H$_3$CH$_2$N), 20.84 (CH_3, Ar*C*H$_3$), 43.6 (CH_2, br, *C*H$_2$N), 103.4 [C, *C*(2)S], 120.7, 124.9, 128.7, 129.2, 129.89 (5 × CH, aromatic *C*H), 133.4, 135.5, 143.7 (3 × C, aromatic *C*), 150.6 [CH, *C*(3)H], 162.2 (C, *C*O).

_N_-(4-Fluorophenyl)-_Z_-3-diethylamino-2-(methylsulfinyl)propenamide 20b-_Z_ and _N_-(4-Fluorophenyl)-_E_-3-diethylamino-2-(methylsulfinyl)propenamide 20b-_E_

This was prepared using the procedure described for **14a** using **18b** (0.24 g, 0.90 mmol), diethylamine (0.23 mL, 2.26 mmol) and CH_2Cl_2 (7 mL). The crude product contained a 3:1 mixture of the *Z* and *E* isomers of **20b**. As this compound decomposed to a black complex mixture of unidentified compounds within 1 h of its preparation, purification and full characterisation was not possible; δ_H (300 MHz, $CDCl_3$) 1.11-1.32 (3H, m, CH_2CH_3), 2.75 (2.25H, s, SC*H*$_3$-*Z*), 2.90 (0.75H, s, SC*H*$_3$-*E*), 3.19-3.31 [0.38H, s, one of $(CH_3)_2$C*H*-*E*], 3.54-3.72 [0.38H, s, one of $(CH_3)_2$C*H*-*E*], 3.33-3.81 (2H, m, NC*H*$_2$), 6.86 [0.25H, s, =C(3)*H*N-*E*], 6.92-7.12 (2H, m, Ar*H*), 7.49-7.59 (2H, m, Ar*H*), 7.70 [0.75H, s, =C(3)*H*N-*Z*], 9.71 (0.25H, br s, N*H*-*E*), 10.37 (0.75H, br s, N*H*-*Z*).

_N_-(4-Benzyl)-_Z_-3-diethylamino-2-(benzylsulfinyl)propenamide 20g-_Z_ and _N_-(4-Benzyl)-_E_-3-diethylamino-2-(benzylsulfinyl)propenamide 20g-_E_

This was prepared using the procedure described for **14a** using **18g** (0.3 g, 0.90 mmol), and diethylamine (4.1 M in ethanol, 4 mL, 16.5 mmol). The reaction was complete after stirring for 15 min at room temperature and the product as a orange oil (0.31 g, 92 %), and as a 5:1

mixture of the *Z* and *E* isomers of **20g**; ν_{max}/cm^{-1} (film) 3410 (NH), 1642 (CO amide), 1029 (SO);

20g-*Z*: δ_H (400 MHz, $CDCl_3$) 0.97 (6H, t, *J* 7.2, C*H*$_3$CH$_2$N), 2.90-3.06 (4H, br m, NC*H*$_2$), 4.27 (1H, d, H_A of AB system, *J* 12.0, one of SC*H*$_2$), 4.37 (1H, d, H_B of AB system, *J* 12.0, one of SC*H*$_2$), 4.52 (1H, A of ABX, J_{AB} 14.7, J_{AX} 5.4, one of NC*H*$_2$Bn), 4.69 (1H, B of ABX, J_{AB} 14.7, J_{AX} 5.4, one of NC*H*$_2$Bn), 7.13-7.47 (10H, m, Ar*H*), 7.74 [1H, s, C(3)*H*], 8.86 (1H, br t, *J* 5.5, N*H*); δ_C (75.5 MHz, $CDCl_3$) 11.3 [*C*H$_3$, 2 × N(CH$_2$*C*H$_3$)$_2$], 42.3 [CH$_2$, 2 × N(*C*H$_2$CH$_3$)], 43.5 (CH$_2$, NH*C*H$_2$), 58.9 (CH$_2$, S*C*H$_2$), 92.1 [C, *C*(2)S], 127.0, 127.7, 128.2, 128.4, 128.6, 128.7, 130.5 (6 × CH, aromatic *C*H), 130.7, 139.4 (2 × C, aromatic *C*), 150.8 [CH, *C*(3)H], 167.9 (C, *C*O).

20g-*E*: δ_H (400 MHz, $CDCl_3$) 1.06 (6H, t, *J* 7.2, C*H*$_3$CH$_2$N), 2.90-3.06 (4H, br m, NC*H*$_2$), 3.99 (2H, s, SC*H*$_2$Bn), 4.43-4.62 (2H, m, NC*H*$_2$Bn), 6.43 [1H, s, C(3)*H*], 7.13-7.47 (10H, m, Ar*H*), 8.20 (1H, br t, *J* 5.8, N*H*); δ_C (75.5 MHz, $CDCl_3$) 11.3 [*C*H$_3$, 2 × N(CH$_2$*C*H$_3$)$_2$], 42.3 [CH$_2$, 2 × N(*C*H$_2$CH$_3$)], 43.5 (CH$_2$, NH*C*H$_2$), 58.4 (CH$_2$, S*C*H$_2$), 98.5 [C, *C*(2)S], 127.0, 127.7, 128.2, 128.4, 128.6, 128.7, 130.5 (6 × CH, aromatic *C*H), 130.7, 138.8 (2 × C, aromatic *C*), 148.8 [CH, *C*(3)H], 164.4 (C, *C*O).

HRMS (ESI+): Exact mass calculated for $C_{21}H_{27}N_2O_2S$ ($M+H^+$). Found ($M+H^+$); m/z (ESI^+) 371.2 ($M+H^+$).

_N_-(4-Methylphenyl)-_Z_-3-dimethylamino-2-(phenylsulfinyl)propenamide 21a-_Z_ and _N_-(4-Methylphenyl)-_E_-3-dimethylamino-2-(phenylsulfinyl)propenamide 21a-_E_

This was prepared using the procedure described for **14a** using **18a** (0.2 g, 0.94 mmol), and dimethylamine (5.6 M in ethanol, 3 mL, 17.0 mmol). After stirring for 15 min at room temperature the reaction was complete by TLC analysis. The product was obtained as a yellow oil (0.19 g, 94 %), as a 1:1.2 mixture of the *Z* and *E* isomers of **21a**; ν_{max}/cm^{-1} (film) 3472 (NH), 1660 (CO amide), 1080 (SO).

21a-*E*: δ_H (400 MHz, $CDCl_3$) 2.22 (3H, s, ArC*H*$_3$), 3.10 [3H, s, one of N(C*H*$_3$)$_2$], 3.25 [3H, s, one of N(C*H*$_3$)$_2$], 6.90-7.64 [10H, m, Ar*H* and C(3)*H*; C(3)*H* can be seen as a singlet at 7.09], 9.08 (1H, s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 20.84 (CH$_3$, Ar*C*H$_3$), 44.0 [*C*H$_3$, 2 × N(*C*H$_3$)$_2$], 103.8 [C, *C*(2)S], 120.6, 124.9, 128.8, 129.2, 130.0 (5 × CH, aromatic *C*H), 133.4, 135.3, 143.5 (3 × C, aromatic *C*), 152.9 [CH, *C*(3)H], 162.0 (C, *C*O).

21a-*Z*: δ_H (400 MHz, $CDCl_3$) 2.22 (3H, s, ArC*H*$_3$), 3.10 [3H, s, one of N(C*H*$_3$)$_2$], 3.25 [3H, s, one of N(C*H*$_3$)$_2$], 6.90-7.64 (9H, m, Ar*H*), 7.95 [1H, s, C(3)*H*], 9.66 (1H, s, N*H*); δ_C (75.5

MHz, $CDCl_3$) 20.80 (CH_3, Ar*C*H_3), 45.6 [*C*H_3, 2 × N(*C*H_3)$_2$], 98.8 [C, *C*(2)S], 120.3, 124.8, 129.1, 129.2, 129.9 (5 × CH, aromatic *C*H), 132.9, 136.1, 144.8 (3 × C, aromatic *C*), 153.6 [CH, *C*(3)H], 165.3 (C, *C*O).

HRMS (ESI+): Exact mass calculated for $C_{17}H_{17}N_2O_2S$ (M-CH_3^-) 313.1011. Found 330.1344 (M-CH_3^-); m/z (ESI$^+$) 313.1 (M-CH_3^-).

_N_-(4-Benzyl)-_Z_-3-dimethylamino-2-(benzylsulfinyl)propenamide 21g-_Z_ and _N_-(4-Benzyl)-_E_-3-dimethylamino-2-(benzylsulfinyl)propenamide 21g-_E_

This was prepared using the procedure described for **14a** using **18g** (0.3 g, 0.90 mmol) and dimethylamine (5.6 M in ethanol, 4 mL, 22.6 mmol). After stirring for 15 min at room temperature the reaction was complete by TLC analysis and the product was obtained as a yellow oil (0.27 g, 89 %), as a 2.9:1 mixture of the *Z* and *E* isomers of **21g**; ν_{max}/cm^{-1} (film) 3396 (NH), 1648 (CO amide), 1028 (SO).

21g-_Z_: δ_H (400 MHz, $CDCl_3$) 2.75 [6H, s, N(C*H*$_3$)$_2$], 4.25 (1H, d, H_A of AB system, *J* 11.9, one of SC*H*$_2$), 4.35 (1H, d, H_B of AB system, *J* 11.9, one of SC*H*$_2$), 4.52 (1H, A of ABX, J_{AB} 15.0, J_{AX} 5.7, one of NC*H*$_2$Bn), 4.69 (1H, B of ABX, J_{AB} 15.0, J_{BX} 5.7, one of NC*H*$_2$Bn), 7.08-7.49 (10H, m, Ar*H*), 7.70 [1H, s, C(3)*H*], 8.84 (1H, bt, *J* 5.5, N*H*); δ_C (75.5 MHz, $CDCl_3$) 43.4 [CH_3, N(*C*H_3)$_2$], 44.9 (CH_2, br, *C*H_2NH), 59.0 (CH_2, S*C*H_2), 94.0 [C, *C*(2)S], 127.0, 127.7, 128.3, 128.6, 128.7, 130.5 (5 × CH, aromatic *C*H), 130.8, 139.3 (2 × C, aromatic *C*), 153.0 [CH, *C*(3)H], 167.6 (C, *C*O).

21g-_E_: δ_H (400 MHz, $CDCl_3$) 2.98 [6H, s, N(C*H*$_3$)$_2$], 3.99 (2H, s, SC*H*$_2$Bn), 4.40-4.71 (2H, m, NC*H*$_2$Bn), 6.51 [1H, s, C(3)*H*], 7.08-7.49 (10H, m, Ar*H*), 8.10 (1H, bt, *J* 5.5, N*H*); δ_C (75.5 MHz, $CDCl_3$) 43.3 [CH_3, N(*C*H_3)$_2$], 43.7 (CH_2, *C*H_2NH), 58.3 (CH_2, S*C*H_2), 99.4 [C, *C*(2)S], 127.3, 127.9, 128.1, 128.66, 128.72, 130.4 (5 × CH, aromatic *C*H), 131.0, 138.8 (2 × C, aromatic *C*), 151.4 [CH, *C*(3)H], 164.3 (C, *C*O).

HRMS (ESI+): Exact mass calculated for $C_{19}H_{23}N_2O_2S$ (M+H^+) 343.1480. Found 343.1480 (M+H^+); m/z (ESI$^+$) 343.2 (M+H^+).

_N_-(4-Methylphenyl)-_Z_-3-piperidino-2-(benzenesulfinyl)propenamide 22a-_Z_ and _N_-(4-Methylphenyl)-_E_-3-piperidino-2-(benzenesulfinyl)propenamide 22a-_E_

This was prepared using the procedure described for **14a** using **18a** (0.25 g, 0.78 mmol), piperidine (0.19 mL, 1.96 mmol) and CH_2Cl_2 (8 mL) to give a 1.7:1 mixture of the *E* and *Z* isomers of **22a**. Following purification on silica gel using hexane:ethyl acetate (40:60) as

eluent, **22a** was isolated as a pale yellow solid (0.17 g, 59%), (ratio of isomers identical following chromatography); mp 126−127 °C; (Found C, 68.05; H, 6.84; N, 7.28; S, 8.69. $C_{21}H_{24}N_2O_2S$ requires C, 68.45; H, 6.56; N, 7.60; S, 8.70%); ν_{max}/cm^{-1} (KBr) 2380, 2341, 1658 (CO), 1601; δ_H (300 MHz, $CDCl_3$) 1.59-1.85 [6H, m, C(3′)H_2, C(4′)H_2, C(5′)H_2 of *Z* and *E*], 2.23 (3H, s, ArCH_3), 3.51 (1.26H, br s, NCH_2-*E*), 3.68 (0.74H, br s, NCH_2-*Z*), 6.91-7.71 [9.63H, m, Ar*H* and =C(3)*H*N-*E*], 7.88 [0.37H, s, =C(3)*H*N-*Z*], 9.12 (0.63H, br s, N*H*-*E*), 9.65 (0.37H, br s, N*H*-*Z*).

22a-*Z* δ_c (75.5 MHz, $CDCl_3$) 20.8 (CH_3, Ar*C*H_3), 23.6 [CH_2, *C*(4′)H_2], 26.5 [CH_2, br, *C*(3′)H_2 and *C*(5′)H_2], 54.6 [CH_2, br, N(*C*H_2)$_2$], 96.7 [C, *C*(2)], 120.3, 124.8, 129.1, 130.0 (CH, aromatic *C*H), 132.8, 136.1, 144.4 (C, aromatic *C*), 152.5 [CH, =*C*(3)HN], 165.5 (C, *C*O);

22a-*E* δ_c (75.5 MHz, $CDCl_3$) 20.8 (CH_3, Ar*C*H_3), 23.5 [CH_2, *C*(4′)H_2], 25.4 [CH_2, br, *C*(3′)H_2 and *C*(5′)H_2], 54.4 [CH_2, br, N(*C*H_2)$_2$], 120.5 [C, *C*(2)], 120.7, 124.9, 129.1, 129.9 (CH, aromatic *C*H), 133.4, 135.2, 143.6 (C, aromatic *C*), 151.5 [CH, =*C*(3)HN], 162.6 (C, *C*O); MS *m/z* 368 (M^+, 6%).

_N_-(4-Fluorophenyl)-_Z_-3-piperidino-2-(methylsulfinyl)propenamide 22b-_Z_ and _N_-(4-Fluorophenyl)-_E_-3-piperidino-2-(methylsulfinyl)propenamide 22b-_E_

This was prepared using the procedure described for **14a** using **18b** (0.10 g, 0.38 mmol), piperidine (0.1 mL, 0.96 mmol) and CH_2Cl_2 (3 mL). The crude product contained a 1.1:1 mixture of the *E* and *Z* isomers of **22b**. As this compound decomposed to a black complex mixture of unidentified compounds within 1 h of its preparation, purification and full characterisation was not possible; δ_H (300 MHz, $CDCl_3$) 1.51-1.86 [6H, m, C(3′)H_2, C(4′)H_2, C(5′)H_2 of *Z* and *E*], 2.72 (1.4H, s, SCH_3-*Z*), 2.75 (1.6H, s, SCH_3-*E*), 3.36-3.69 (4H, m, NCH_2 of *Z* and *E*), 6.83 [0.47H, s, =C(3)*H*N-*Z*], 6.92-7.12 (2H, m, Ar*H*), 7.49-7.61 [2.53H, m, Ar*H* and =C(3)*H*N-*E*], 9.72 (0.53H, br s, N*H*-*E*), 10.37 (0.47H, br s, N*H*-*Z*).

_N_-(4-Methylphenyl)-_Z_-3-morpholino-2-(benzenesulfinyl)propenamide 23a-_Z_ and _N_-(4-Methylphenyl)-_E_-3-morpholino-2-(benzenesulfinyl)propenamide 23a-_E_

This was prepared following the procedure described for **14a** using **18a** (0.30 g, 0.94 mmol) in CH_2Cl_2 (10 mL) and morpholine (0.21 mL, 2.35 mmol). TLC analysis indicated that the reaction was complete after 5 min. Following purification by chromatography using hexane:ethyl acetate (40:60), the adduct (0.22 g, 64%) was obtained as a yellow solid and an inseparable mixture of *E* and *Z* isomers in a ratio of 3:1 respectively, mp 56−60 °C; (Found

C, 64.72; H, 6.18; N, 7.78; S, 9.05. $C_{20}H_{22}N_2O_3S$ requires C, 64.84; H, 5.98; N, 7.56; S, 8.65%); ν_{max}/cm^{-1} (KBr) 3338 (NH), 1654 (CO), 1522 (NH bend), 817; δ_H (300 MHz, $CDCl_3$) 2.24 (3H, s, ArC*H*$_3$ of *E* and *Z*), 3.41-3.89 [8H, m, N(C*H*$_2$C*H*$_2$)$_2$O of *E* and *Z*], 6.91-7.15 (4H, m, Ar*H*), 7.12-7.51 [3.75H, m, Ar*H* and =C(3)*H*N-*E*], 7.52-7.68 (2H, m, Ar*H*), 7.91 [1H, s,=C(3)*H*N-*Z*], 9.20 (0.75H, br s, N*H*-*E*), 9.62 (0.25, br s, N*H*-*Z*);

23a-*E*: δ_c (75.5 MHz, $CDCl_3$) 21.2 (CH_3, Ar*C*H$_3$), 53.0 [CH_2, br, N*C*(2′)H$_2$ & N*C*(6′)H$_2$], 66.9 [CH_2, O*C*(3′)H$_2$ & O*C*(5′)H$_2$], 104.5 [C, *C*(2)S], 121.1, 125.2, 129.6, 130.6, 132.2 (5 × CH, 5 × aromatic *C*H), 134.2, 135.4, 143.6 (C, aromatic *C*), 151.5 [CH, *C*(3)H=], 162.6 (C, *C*O).

23a-*Z*: δ_c (75.5 MHz, $CDCl_3$) 21.2 (CH_3, Ar*C*H$_3$), 52.2 [CH_2, br, N*C*(2′)H$_2$ & N*C*(6′)H$_2$], 66.9 [CH_2, O*C*(3′)H$_2$ & O*C*(5′)H$_2$], 99.0 [C, *C*(2)S], 120.8, 125.1, 129.3, 130.5, 132.3 (5 × CH, 5 × aromatic *C*H), 133.0, 136.3, 144.2 (C, aromatic *C*), 152.8 [CH, *C*(3)H=], 166.1 (C, *C*O); MS *m/z* 264 (M^+ – CONHTol, 32%).

_N_-Ethyl-_Z_-3-morpholino-2-(benzenesulfinyl)propenamide 23c-_Z_ and _N_-Ethyl-_E_-3-morpholino-2-(benzenesulfinyl)propenamide 23c-_E_

This was prepared following the procedure described for **14a** using **18c** (0.25 g, 0.97 mmol) in CH_2Cl_2 (5 mL) and morpholine (0.23 mL, 2.43 mmol). Following purification by chromatography using hexane:ethyl acetate (40:60), the adduct (0.22 g, 64%) was obtained as a yellow solid and an inseparable mixture of *E* and *Z* isomers in a ratio of 3.8:1 respectively, mp 60−63 °C; (Found C, 57.96; H, 6.64; N, 8.76; S, 10.00. $C_{15}H_{20}N_2O_3S$ requires C, 58.42; H, 6.54; N, 9.08; S, 10.40%); ν_{max}/cm^{-1} (KBr) 1639 (CO), 1443, 991; δ_H (300 MHz, $CDCl_3$) 0.69 (4.75H, t, *J* 7.3, CH_2CH_3 of *E*), 0.77 (1.25H, t, *J* 7.3, CH_2CH_3 of *Z*), 2.78-3.26 (2H, m, CH_2CH_3 of *E* and *Z*), 3.39-3.91 [8H, m, N(C*H*$_2$C*H*$_2$)$_2$O of *E* and *Z*], 6.95 [0.79H, s, =C(3)*H*N of *E*], 7.18-7.71 (5H, m, Ar*H*), 7.83 [1H, s,=C(3)*H*N-*Z*];

23c-*E*: δ_c (75.5 MHz, $CDCl_3$) 14.2 (CH_3, CH_2CH_3), 33.8 (CH_2, CH_2CH_3), 51.5 [CH_2, br, N*C*(2′)H$_2$ & N*C*(6′)H$_2$], 66.5 [CH_2, O*C*(3′)H$_2$ & O*C*(5′)H$_2$], 104.2 [C, *C*(2)S], 125.2, 128.7, 129.6 (3 × CH, 3 × aromatic *C*H), 142.2 (C, aromatic *C*), 151.0 [CH, *C*(3)H=], 163.8 (C, *C*O).

23c-*Z*: δ_c (75.5 MHz, $CDCl_3$) 14.5 (CH_3, CH_2CH_3), 33.8 (CH_2, CH_2CH_3), 52.4 [CH_2, br, N*C*(2′)H$_2$ & N*C*(6′)H$_2$], 66.3 [CH_2, O*C*(3′)H$_2$ & O*C*(5′)H$_2$], 99.5 [C, *C*(2)S], 124.9, 129.0, 129.2 (3 × CH, 3 × aromatic *C*H), 143.5 (C, aromatic *C*), 152.2 [CH, *C*(3)H=], 166.2 (C, *C*O); MS *m/z* 290 (90%), 262 (70%), 218 (100%).

_N_-(4-Fluorophenyl)-_Z_-3-morpholino-2-(methylsulfinyl)propenamide 23b-_Z_ and _N_-(4 -Fluorophenyl)-_E_-3-morpholino-2-(methylsulfinyl)propenamide 23b-_E_

This was prepared following the procedure described for **14a** using **18b** (0.15 g, 0.58 mmol) in CH_2Cl_2 (4 mL) and morpholine (0.15 mL, 1.40 mmol). Following purification by chromatography using hexane:ethyl acetate (40:60), the adduct (0.11 g, 65%) was obtained as a yellow sticky solid and an inseparable equimolar mixture of *E* and *Z* isomers, mp 58−62 °C; (Found C, 52.44; H, 5.45; N, 8.35. $C_{14}H_{17}N_2O_3SF.H_2O$ requires C, 52.38; H, 5.60; N, 8.72%); ν_{max}/cm^{-1} (KBr) 3336, 2927, 1651 (CO), 1532, 1028; δ_H (300 MHz, $CDCl_3$) 2.77 (1.5H, s, SC*H*$_3$ of *Z*), 2.89 (1.5H, s, SC*H*$_3$ of *E*), 3.39-3.83 [8H, m, N(C*H*$_2$C*H*$_2$)$_2$O of *E* and *Z*], 6.82 [0.5H, s, =C(3)*H*N-*E*], 6.91-7.09 (2H, m, Ar*H*), 7.51-7.69 [2.5H, m, Ar*H* and =C(3)*H*N-*Z*], 9.78 (0.5H, br s, N*H*-*Z*), 10.29 (0.5H, br s, N*H*-*E*);

23b-*E*: δ_c (75.5 MHz, $CDCl_3$) 39.2 (CH_3, S*C*H$_3$), 51.7 [CH_2, br, N*C*(2′)H$_2$ & N*C*(6′)H$_2$], 66.3 [CH_2, O*C*(3′)H$_2$ & O*C*(5′)H$_2$], 101.8 [C, *C*(2)S], 115.7 [CH, d, $^2J_{CF}$ 22, aromatic *C*(3)H], 122.0 [CH, d, $^3J_{CF}$ 8, aromatic *C*(2)H], 134.1 [C, d, $^4J_{CF}$ 3, aromatic *C*(1)], 150.6 [CH, *C*(3)H=], 163.8 (C, *C*O).

23b-*Z*: δ_c (75.5 MHz, $CDCl_3$) 39.7 (CH_3, S*C*H$_3$), 51.4 [CH_2, br, N*C*(2′)H$_2$ & N*C*(6′)H$_2$], 66.2 [CH_2, O*C*(3′)H$_2$ & O*C*(5′)H$_2$], 98.1 [C, *C*(2)S], 115.4 [CH, d, $^2J_{CF}$ 22, aromatic *C*(3)H], 121.9 [CH, d, $^3J_{CF}$ 8, aromatic *C*(2)H], 134.1 [C, d, $^4J_{CF}$ 3, aromatic *C*(1)], 150.1 [CH, *C*(3)H=], 166.3 (C, *C*O); MS *m/z* 328 ($M^+ + H_2O$, 1%), 256 (100%).

_N_-(4-Fluorophenyl)-_Z_-3-morpholino-2-(benzylsulfinyl)propenamide 23d-_Z_ and _N_-(4 -Fluorophenyl)-_E_-3-morpholino-2-(benzylsulfinyl)propenamide 23d-_E_

The title compound was prepared as described for **14a** using **18d** (0.16 g, 0.5 mmol) in CH_2Cl_2 (5 mL) and morpholine (0.10 mL, 1.2 mmol). The reaction mixture was stirred for 5 min and then checked for completion by TLC. Following the work-up, the adduct was obtained (0.16 g, 87%) as a white solid, mp 61−62 °C, which required no further purification and as an inseparable mixture of *E* and *Z* isomers in a ratio of 1:2.4 respectively; ν_{max}/cm^{-1} (KBr) 3456 (NH), 3236 (NH), 3032 (CH), 2922 (CH), 1659 (CO), 1614, 1589 (NH bend), 1508, 1068 (SO);

Minor isomer **23d**-*E*; δ_H (300 MHz, $CDCl_3$) 3.05-3.78 [8H, m, N(C*H*$_2$C*H*$_2$)$_2$O]*, 4.20 (2H, d, *J* 2.1, SC*H*$_2$), 6.45 [1H, s, C(3)*H*=], 6.98-7.65 (9H, m, Ar*H*)*, 9.99 (1H, br s, N*H*); δ_c (75.5 MHz, $CDCl_3$) 52.1 [CH_2, br, N*C*(2″)H$_2$ & N*C*(6″)H$_2$], 59.0 (CH_2, S*C*H$_2$), 66.6 [CH_2,

O*C*(3″)H_2 & O*C*(5″)H_2], 98.3 [C, *C*(2)S], 115.6 [CH, d, $^2J_{CF}$ 23, aromatic *C*(3′)H], 121.9 [CH, d, $^3J_{CF}$ 8, aromatic *C*(2′)H], 128.2, 128.8, 130.5 (3 × CH, 3 × aromatic *C*H), 134.3 (C, aromatic *C*), 149.8 [CH, *C*(3)H=], 159.2 [C, d, $^1J_{CF}$ 243, Ar*C*(4′)], 162.6 (C, *C*O).

Major isomer **23d**-*Z*; δ_H (300 MHz, $CDCl_3$) 3.05-3.78 [8H, m, N(CH_2CH_2)$_2$O]*, 4.35 (1H, A of ABq, *J* 12.0, one of SCH_2), 4.44 (1H, B of ABq, *J* 11.7, one of SCH_2), 6.96-7.63 (9H, m, Ar*H*)*, 7.68 [1H, s, C(3)*H*=], 10.56 (1H, br s, N*H*); δ_c (75.5 MHz, $CDCl_3$) 52.2 [CH_2, br, N*C*(2″)H_2 & N*C*(6″)H_2], 59.4 (CH_2, S*C*H_2), 65.9 [CH_2, O*C*(3″)H_2 & O*C*(5″)H_2], 93.1 [C, *C*(2)S], 115.5 [H, d, $^2J_{CF}$ 22, aromatic *C*(3′)H], 121.9 [CH, d, $^3J_{CF}$ 8, aromatic *C*(2′)H], 128.6, 128.9, 130.5 (3 × CH, 3 × aromatic *C*H), 134.9 (C, aromatic *C*), 152.1 [CH, *C*(3)H=], 158.9 [C, d, $^1J_{CF}$ 243, aromatic *C*(4′)], 165.4 (C, *C*O).

*These signals for the two isomers could not be distinguished

HRMS (ES+): Exact mass calculated for $C_{20}H_{22}N_2O_3SF$ $[M+H]^+$ 389.1335. Found 389.1337; *m/z* (ES+) 389.2 {[($C_{20}H_{21}N_2O_3SF$)+H^+], 100%}.

_N_-_n_-Butyl-_Z_-3-morpholino-2-(benzylsulfinyl)propenamide 23e-_Z_ and _N_-_n_-butyl-_E_-3-morpholino-2-(benzylsulfinyl)propenamide 23e-_E_

This was prepared as outlined for **14a** using **18e**-*E* (0.10 g, 0.32 mmol) in CH_2Cl_2 (5 mL) and morpholine (0.07 mL, 0.79 mmol). The reaction was complete by TLC analysis after 5 min and following the work-up, the sulfoxide adduct was obtained as a colourless oil and an inseparable mixture of *E* and *Z* isomers in a ratio of 1:1 respectively. Following purification using hexane-ethyl acetate (gradient elution 80-100% ethyl acetate) as eluent, the adduct was obtained as a colourless oil and as an inseperable mixture of *E* and *Z* isomers in a ratio 1:1.6 respectively (0.08 g, 67%); ν_{max}/cm^{-1} (KBr) 3468 (NH), 3266 (NH), 3031 (CH), 2960 (CH), 1645 (CO), 1589, 1454 (CN stretch), 1069 (SO).

Minor isomer **23e**-*E*; δ_H (300 MHz, $CDCl_3$) 0.96 [3H, t, *J* 7.2, C(4′)H_3]*, 1.36-1.67 [4H, m, C(3′)H_2 & C(2′)H_2]*, 3.01-3.76 [8H, m, N(CH_2CH_2)$_2$O]*, 4.14 (2H, s, SCH_2), 6.37 [1H, s, C(3)*H*=], 7.21-7.39 (5H, m, Ar*H*)*, 7.83 (1H, br s, N*H*); δ_c (75.5 MHz, $CDCl_3$) 14.2 [CH_3, *C*(4′)H_3], 20.7 [CH_2, *C*(3′)H_2], 32.2 [CH_2, *C*(2′)H_2], 39.5 (CH_2, *C*H_2NH), 52.0 (CH_2, S*C*H_2), 58.9 [CH_2, N*C*(2″)H_2 & N*C*(6″)H_2], 67.0 [CH_2, O*C*(3″)H_2 & O*C*(5″)H_2], 100.1 [C, *C*(2)S], 128.4, 128.8, 129.1, 129.2 (4 × CH, 4 × aromatic *C*H)*, 130.6 (C, aromatic *C*)*, 130.9, 131.1 (2 × CH, 2 × aromatic *C*H)*, 131.3 (C, aromatic *C*)*, 149.2 [CH, *C*(3)H=], 164.8 (C, *C*O);

Major isomer **23e**-*Z*; δ_H (300 MHz, $CDCl_3$) 0.96 [3H, t, *J* 7.3, C(4′)H_3]*, 1.36-1.67 [4H, m, C(3′)H_2 and C(2′)H_2]*, 3.01-3.76 [8H, m, N(CH_2CH_2)$_2$O]*, 4.27 (1H, A of ABq, *J* 11.7, one of SCH_2), 4.44 (1H, B of ABq, *J* 11.7, one of SCH_2), 7.21-7.39 (5H, m, Ar*H*)*, 7.61 [1H, s, C(3)*H*=], 8.39 (1H, br t, N*H*); δ_c (75.5 MHz, $CDCl_3$) 14.2 [CH_3, *C*(4′)H_3], 20.8 [CH_2, *C*(3′)H_2], 32.3 [CH_2, *C*(2′)H_2], 39.7 (CH_2, *C*H_2NH), 52.3 (CH_2, S*C*H_2), 59.1 [CH_2, N*C*(2″)H_2 & N*C*(6″)H_2], 66.3 [CH_2, O*C*(3″)H_2 & O*C*(5″)H_2], 94.0 [C, *C*(2)S], 128.4, 128.8, 129.1, 129.2 (4 × CH, 4 × aromatic *C*H)*, 130.6 (C, aromatic *C*)*, 130.9, 131.1 (2 × CH, 2 × aromatic *C*H)*, 131.3 (C, aromatic *C*)*, 152.1 [CH, *C*(3)H=], 167.5 (C, *C*O);

* The *n*-butyl and aromatic signals could not be distinguished for the two isomers.

HRMS (ES+): Exact mass calculated for $C_{18}H_{27}N_2O_3S$ $[M+H]^+$ 351.1742. Found 351.1729; *m/z* (ES+) 351.1 {[($C_{18}H_{26}N_2O_3S$)+H^+], 100%}.

This reaction was also conducted using **18e**-*Z* (0.12 g, 0.4 mmol) in CH_2Cl_2 (5 mL) and morpholine (0.08 mL, 1.0 mmol). The reaction was complete by TLC analysis after 5 min and following the work-up, the adduct (0.11 g, 80%) was obtained as a yellow oil and an inseparable mixture of *E* and *Z* isomers in a ratio of 1:1.6 respectively. Further purification was not required; ν_{max}/cm^{-1} (KBr) 3468 (NH), 3266 (NH), 3031 (CH), 2960 (CH), 1645 (CO), 1589, 1454 (CN stretch), 1069 (SO).

Minor isomer **23e**-*E*; δ_H (300 MHz, $CDCl_3$) 0.96 [3H, t, *J* 7.2, C(4′)H_3]*, 1.36-1.67 [4H, m, C(3′)H_2 & C(2′)H_2]*, 3.01-3.76 [8H, m, N(CH_2CH_2)$_2$O]*, 4.14 (2H, s, SCH_2), 6.37 [1H, s, C(3)*H*=], 7.21-7.39 (5H, m, Ar*H*)*, 7.83 (1H, br s, N*H*);

Major isomer **23e**-*Z*; δ_H (300 MHz, $CDCl_3$) 0.96 [3H, t, *J* 7.3, C(4′)H_3]*, 1.36-1.67 [4H, m, C(3′)H_2 & C(2′)H_2]*, 3.01-3.76 [8H, m, N(CH_2CH_2)$_2$O]*, 4.27 (1H, A of ABq, *J* 11.7, one of SCH_2), 4.44 (1H, B of ABq, *J* 11.7, one of SCH_2), 7.21-7.39 (5H, m, Ar*H*)*, 7.61 [1H, s, C(3)*H*=], 8.39 (1H, br t, N*H*);

*The *n*-butyl and aromatic signals could not be distinguished for the two isomers.

_N_-(4-Methylphenyl)-_Z_-3-morpholino-2-(benzylsulfinyl)propenamide 23f-_Z_ and _N_-(4-Methylphenyl)-_E_-3-morpholino-2-(benzylsulfinyl)propenamide 23f-_E_

This was prepared following the procedure described for **14a** using **18f** (0.10 g, 0.3 mmol) in dichloromethane (10 mL) and morpholine (0.06 mL, 0.7 mmol). TLC analysis indicated that the reaction was complete after 10 min and the adduct (0.09 g, 85%) was obtained as a brown solid and an inseparable mixture of *E* and *Z* isomers in a ratio of 1:1.9 respectively, mp 139−140 °C. Further purification was not required; ν_{max}/cm^{-1} (KBr) 3266 (NH), 3214 (NH),

3030 (CH), 1656 (CO), 1603, 1544 (NH bend), 1513, 1444 (CN stretch), 1069 (SO); Minor isomer **23f**-*E*; δ_H (300 MHz, $CDCl_3$) 2.33 (3H, s, ArC*H*$_3$)*, 3.04-3.77 [8H, m, (N(C*H*$_2$C*H*$_2$)$_2$O]*, 4.20 (2H, s, SC*H*$_2$), 6.45 [1H, s, C(3)*H*=], 7.11-7.59 (9H, m, Ar*H*)*, 9.88 (1H, br s, N*H*); δ_c (75.5 MHz, $CDCl_3$) 21.3 (CH_3, Ar*C*H$_3$), 52.3 [CH_2, br, N*C*(2′)H$_2$ & N*C*(6′)H$_2$], 59.2 (CH_2, S*C*H$_2$), 67.0 [CH_2, O*C*(3′)H$_2$ & O*C*(5′)H$_2$], 99.3 [C, *C*(2)S], 120.8, 128.5, 129.0, 129.1, 129.3, 129.8, 129.9 (7 × CH, 7 × aromatic *C*H)*, 130.4 (C, aromatic *C*)*, 130.9, (CH, aromatic *C*H)*, 131.0 (C, aromatic *C*)*, 131.1 (CH, aromatic *C*H)*, 134.2, 136.1 (2 × C, 2 × aromatic *C*), 150.2 [CH, *C*(3)H=], 162.9 (C, *C*O).

Major isomer **23f**-*Z*; δ_H (300 MHz, $CDCl_3$) 2.33 (3H, s, ArC*H*$_3$)*, 3.04-3.779 [8H, m, N(C*H*$_2$C*H*$_2$)$_2$O]*, 4.35 (1H, A of ABq, *J* 12.0, one of SC*H*$_2$), 4.45 (1H, B of ABq, *J* 12.0, one of SC*H*$_2$), 7.11-7.59 (9H, m, Ar*H*)*, 7.67 [1H, s, C(3)*H*=], 10.49 (1H, br s, N*H*); δ_c (75.5 MHz, $CDCl_3$) 21.3 (CH_3, Ar*C*H$_3$), 52.5 [CH_2, br, N*C*(2′)H$_2$ & N*C*(6′)H$_2$], 59.6 (CH_2, S*C*H$_2$), 66.3 [CH_2, O*C*(3′)H$_2$ & O*C*(5′)H$_2$], 93.7 [C, *C*(2)S], 120.8, 128.5, 129.0, 129.1, 129.3, 129.8, 129.9 (7 × CH, 7 × aromatic *C*H)*, 130.4 (C, aromatic *C*)*, 130.9, (CH, aromatic *C*H)*, 131.0 (C, aromatic *C*)*, 131.1 (CH, aromatic *C*H)*, 133.5, 136.7 (2 × C, 2 × aromatic *C*), 152.5 [CH, *C*(3)H=], 165.7 (C, *C*O).

*These signals could not be distinguished for the two isomers.

HRMS (ES+): Exact mass calculated for $C_{21}H_{25}N_2O_3S$ $[M+H]^+$ 385.1586. Found 385.1588; *m/z* (ES+) 385.2 {[($C_{21}H_{24}N_2O_3S$)+H^+], 38%}.

_N_-Methyl-_E_-3-morpholino-2-(benzenesulfonyl)propenamide 24a

The stereochemistry was determined by single crystal X-ray diffraction on a crystalline sample of **24a** recrystallised from dichloromethane/hexane. Crystals of **24a** are triclinic, space group *P*-1, formula $C_{14}H_{18}N_2O_4S$, M = 310.36, a = 5.6949(16) Å, b = 9.6545(13) Å, c = 13.611(2) Å, α = 73.20(3) °, β = 83.98(4) °, γ = 80.88(4) °, U = 706.0(2) Å^3, F(000) = 328, μ(Mo-Kα) = 0.247 mm^{-1}, R(F_o) = 0.0683, for 2176 observed reflections with I>2σ(I), wR_2(F^2) = 0.1817 for all 2509 unique reflections. Data in the θ range 2.34-25.39 ° were collected at 125 K on a Rigaku Saturn 724 CCD diffractometer using Mo-Kα graphite monochromated radiation, λ = 0.7107 Å, and corrected for Lorentz and polarization effects. The structure was solved by direct methods and refined by full-matrix least-squares using all F^2 data. The hydrogen atoms were placed in calculated positions and allowed to ride on the parent atom.

_N_-(4-Methylphenyl)-3-_N′_-methylamino-2-(phenylthio)propenamide 25a

Methylamine (12 M in water, 136 μl, 1.1 mmol) was added to a solution of **1a** (150 mg, 0.5 mmol), in CH_2Cl_2 (3 mL) while stirring. The reaction was complete after 5 min by TLC analysis. CH_2Cl_2 (5 mL) and saturated aqueous ammonium chloride (2 mL) were added, the phases were separated and the aqueous layer was washed with CH_2Cl_2 (2 × 10 mL). The combined organic layers were washed with brine (2 × 10 mL), dried (ethanol was necessary to wash the compound from $MgSO_4$) and evaporated to give propenamides **25a-***E/Z* (170 mg) as a yellow, crystalline solid. The *Z* isomer interconverts slowly, on standing or on silica gel, with the *E* isomer (2D TLC analysis). Purification by chromatography using ethyl acetate-hexane (20:80) elutes the less polar **25a-***E* [rf 0.6 using ethyl acetate-hexane (25:75)], (tentatively assigned) *Note:* The *E* and *Z* isomers interconvert on silica gel (2 D analysis) and slowly on standing at room temperature. Thus, a pure sample of one isomer could not be obtained; mp 135−138 °C; (Found C, 68.01; H, 6.08; N, 9.22; S, 10.65. $C_{17}H_{18}N_2OS$ requires C, 68.43; H, 6.08; N, 9.39; S, 10.75); ν_{max}/cm^{-1} (KBr) 3359 (sharp NH), 1651, 1586 (CO α,β-unsaturated amide); δ_H (270 MHz, $CDCl_3$) 2.27 (3H, s, ArC*H*$_3$), 3.02 (3H, d, *J* 5, C*H*$_3$N), 7.04-7.41 (10H, m, Ar*H*, C*H*=), 8.34 (1H, br s N*H*Tol), 9.03-9.20 (1H, br m, N*H*C=); δ_C (67.8 MHz, $CDCl_3$) (As a mixture of *E* and *Z* isomers. The signals corresponding to the major isomer are indicated by the symbol ◊); 20.7 (Ar*C*H$_3$), 35.4$^{◊}$, 35.6 (N*C*H$_3$), 82.8$^{◊}$, 86.0 (*C*S=), 119.7, 119.9$^{◊}$, 124.9$^{◊}$, 125.2 (aromatic *C*H), 125.6, 129.2, 129.7$^{◊}$ (aromatic *C*H), 132.8, 133.0$^{◊}$, 135.5, 135.8$^{◊}$, 136.2, 139.8$^{◊}$ (aromatic *C*), 154.7, 160.9$^{◊}$ (N*C*H=), 165.2, 168.5$^{◊}$ (*C*O); MS *m/z* 298 (M^+, 41 %), 254 (14), 192 (57), 149 (47), 107 (100), and neat ethanol elutes the more polar **25a-***Z* (rf 0.2) (tentatively assigned); δ_H (270 MHz, $CDCl_3$) 2.28 (3H, s, ArC*H*$_3$), 3.06 (3H, d, *J* 5, C*H*$_3$N), 5.40-5.60 (1H, br m, N*H*C=), 7.05-7.41 (9H, m, Ar*H*), 8.22 (1H, d, *J* 14, C*H*=), 8.39 (1H, br s, N*H*).

_N_-[(_S_)-1-Phenylethyl]-3-(1-phenylethylamino)-2-(phenylthio)propenamide 26b

This was prepared following the procedure described for **24a** using racemic (±)-α-methylbenzylamine (0.16 mL, 1.26 mmol) and **1b** (0.20 g, 0.63 mmol) in CH_2Cl_2 (4 mL). The reaction was complete by TLC analysis after stirring at room temperature for 22 h and was quenched with water (10 mL). The crude ratio of *E* & *Z* isomers was 3:1 by integration of the 60 MHz ^{1}H NMR spectrum. Purification by chromatography using ethyl acetate-hexane (10:90) eluted a fraction which was predominantly the *E* isomer with traces of the *Z* isomer [rf 0.6 using ethyl acetate-hexane (25:75) as eluent] (tentatively assigned) (120 mg,

47%) as a colourless oil and an equimolar mixture of diastereomers; ν_{max}/cm^{-1} (film) 3391 (sharp NH), 3264 (br NH), 1627, 1583 (CO α,β-unsaturated amide); δ_H (270 MHz, $CDCl_3$) 1.34, 1.35 [3H, d, *J* 7, C(2)*H*$_3$], 1.52, 1.53 [3H, d, *J* 7, C(2′)*H*$_3$], 4.35-4.49 [1H, m, C(1′)*H*], 5.06 [1H, m, C(1)*H*], 6.85 (1H, br d, *J* 7, N*H*CO) 7.05-7.36 (16H, m, Ar*H*, C*H*=), 9.43 (1H, dd, *J* 13, 7, N*H*C=); δ_C (67.8 MHz, $CDCl_3$) 22.7, 23.5 [*C*(2)H$_3$ and *C*(2′)H$_3$], 48.3 [*C*(1)H], 55.4, 57.5 [*C*(1′)H], 84.0 (S*C*=), 125.1, 125.1, 125.6, 126.0, 126.7, 127.5, 128.3, 128.7 (aromatic *C*H), 139.7, 143.3, 143.4 (aromatic *C*), 157.2 (*C*H=), 168.9 (*C*O); MS *m/z* 402 (M^+, 3 %), 105 (100, $[CH_3CHPh]^+$), 77 (23), and CH_2Cl_2 eluted a fraction which was predominantly the *Z* isomer (rf 0.1) with traces of the *E* isomer (tentatively assigned) (24 mg, 10 %) as a yellow oil and an equimolar mixture of diastereomers; ν_{max}/cm^{-1} (film) 3391 (sharp NH), 3272 (br NH), 1629, 1582 (CO α,β-unsaturated amide); δ_H (270 MHz, $CDCl_3$) 1.38, 1.39 [3H, d, *J* 7, C(2)*H*$_3$], 1.48, 1.49 [3H, d, *J* 8, C(2′)*H*$_3$], 4.49-4.57 [1H, dq, *J* 7, 7, C(2′)*H*], 5.04-5.24 [1H, dq, *J* 7, 8, C(2)*H*], 5.68 (1H, dd, *J* 15, 6, N*H*C=), 6.83 (1H, br d, *J* 7, N*H*CO) 7.05-7.28 (16H, m, Ar*H*, N*H*CO), 8.18 (1H, d, *J* 14, C*H*=); δ_C (67.8 MHz, $CDCl_3$) (as a mixture with *E* isomer) 22.4, 23.3 [*C*(2)H$_3$ and *C*(2′)H$_3$], 48.7 [*C*(1)H], 56.7 [*C*(1′)H], 87.7 (S*C*=), 124.98-129.29 (aromatic *C*H indistinguishable), 135.7, 143.2, 144.1 (aromatic *C*), 151.4 (*C*H=), 166.1 (*C*O); MS *m/z* 402 (M^+, 17 %), 370 (2), 120 (26), 105 (100), 77 (38); Found (HRMS, EI) M^+ 402.17841 $C_{25}H_{26}NOS$ requires *m/z* 402.17659.

_N_-(4-Methylphenyl)-_E_-methylamino-2-(benzenesulfinyl)propenamide 27a

The title compound was prepared according to the procedure outlined for **24a** using **18a** (0.25 g, 0.78 mmol), methylamine (12 M in water, 0.16 mL, 1.95 mmol) and CH_2Cl_2 (8 mL). The crude product was purified on silica gel using hexane:ethyl acetate (40:60) to give **27a** as a white crystalline solid (0.15 g, 60%), mp 124−126 °C; (Found C, 64.39; H, 5.76; N, 9.19; S, 10.24. $C_{17}H_{18}N_2O_2S$ requires C, 64.90; H, 5.77; N, 8.90; S, 10.20%); ν_{max}/cm^{-1} (KBr) 3288, 1651; δ_H (270 MHz, $CDCl_3$) 2.25 (3H, s, ArC*H*$_3$), 3.10 (3H, d, *J* 5.0, NC*H*$_3$), 7.04 (2H, d, *J* 7.0, Ar*H*), 7.13-7.53 [6H, m, C(3)*H*N= and Ar*H*], 7.61 (2H, d, *J* 7.0, Ar*H*), 8.77 (1H, br d, *J* 7.9, N*H*CH$_3$), 9.30 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 20.8 (CH_3, Ar*C*H$_3$), 35.6 (CH_3, N*C*H$_3$), 99.2 (C, S*C*=), 120.3, 124.7, 129.0, 129.2, 130.0 (CH, aromatic *C*H), 133.3, 135.3, 144.7 (C, aromatic *C*), 155.2 [CH, *C*(3)HN=], 165.5 (C, *C*O); MS *m/z* 314 (M^+, 2%), 298 (100%).

_N_-Ethyl-_E_-methylamino-2-(benzenesulfinyl)propenamide 27c

The title compound was prepared according to the procedure outlined for **24a** using **18c** (0.30 g, 1.17 mmol), methylamine (12 M in water, 0.24 mL, 2.92 mmol) and CH_2Cl_2 (9 mL). The crude product was purified by trituration to give **27c** as a white crystalline solid (0.27 g, 93%), mp 139−141 °C; (Found C, 56.70; H, 6.40; N, 10.93; S, 12.42. $C_{12}H_{16}N_2O_2S$ requires C, 56.12; H, 6.39; N, 11.10; S, 12.71%); ν_{max}/cm^{-1} (KBr) 3304, 1643, 1546, 1011; δ_H (270 MHz, $CDCl_3$) 0.82 (3H, t, *J* 7.3, CH_2CH_3), 2.91-3.36 (5H, m, $NHCH_2CH_3$ and NCH_3), 7.05-7.21 [2H, m, C(3)*H*N= and $NHCH_3$], 7.32-7.62 (5H, m, Ar*H*), 8.60 (1H, br s, $NHCH_2CH_3$); δ_C (67.8 MHz, $CDCl_3$) 14.6 (CH_3, CH_2CH_3), 33.1 (CH_2, NCH_2), 35.4 (CH_3, NCH_3), 99.5 (C, S*C*=), 124.9, 128.7, 129.8 (CH, aromatic *C*H), 144.9 (C, aromatic *C*), 154.9 [CH, *C*(3)HN=], 166.9 (C, *C*O); MS *m/z* 252 (M^+, 2%), 44 (100%).

_N_-(4-Methylphenyl)-_E_-isopropylamino-2-(benzenesulfinyl)propenamide 28a

The title compound was prepared according to the procedure outlined for **24a** using **18a** (0.25 g, 0.82 mmol), isopropylamine (0.21 mL, 2.06 mmol) and CH_2Cl_2 (8 mL). The crude product was purified on silica gel using hexane:ethyl acetate (40:60) to give **28a** as a white crystalline solid (0.22 g, 81%), mp 115−117 °C; (Found C, 66.82; H, 6.49; N, 8.30; S, 11.35. $C_{19}H_{22}N_2O_2S$ requires C, 66.83; H, 6.20; N, 8.20; S, 11.44%); ν_{max}/cm^{-1} (KBr) 1648, 1613, 1545, 1253, 1008; δ_H (270 MHz, $CDCl_3$) 1.21-1.41 [6H, m, $(CH_3)_2CH$], 2.25 (3H, s, $ArCH_3$), 3.49-3.69 [1H, m, $(CH_3)_2CH$], 7.01 (2H, d, *J* 8.2, Ar*H*), 7.12-7.50 [6H, m, C(3)*H*N= and Ar*H*], 7.59 (2H, d, *J* 8.2, Ar*H*), 8.75-8.99 [H, br m, $NH(CH_3)_2CH$], 9.25 (1H, br s, N*H*Tol); δ_C (67.8 MHz, $CDCl_3$) 20.8 (CH_3, $ArCH_3$), 23.5 [CH_3, $(CH_3)_2CH$], 23.9 [CH_3, $(CH_3)_2CH$], 50.8 [CH, $(CH_3)_2CH$], 98.7 (C, S*C*=), 120.4, 124.7, 129.0, 129.3, 130.0 (CH, aromatic *C*H), 133.4, 135.2, 144.7 (C, aromatic *C*), 155.2 [CH, *C*(3)HN=], 165.6 (C, *C*O); MS *m/z* 342 (M^+, 15%), 107 (100%).

Addition of ammonia

_N_-Ethyl-_E_-3-amino-2-(benzenesulfinyl)propenamide 32c

This was prepared following the procedure outlined for **24a** using **18c** (0.20 g, 0.78 mmol), aqueous ammonia (20.5 M, 0.1 mL, 1.94 mmol) and acetone (5 mL). After stirring at room temperature for 16 hours, the reaction was complete by TLC analysis. The crude product was purified by chromatography on silica gel using hexane:ethyl acetate (60:40) as eluent to give **31c** as a white crystalline solid (96 mg, 52%); mp 86−88 °C; (Found C, 54.80; H, 5.85; N, 11.60. $C_{19}H_{22}N_2O_2S$ requires C, 55.44; H, 5.92; N, 11.76%); ν_{max}/cm^{-1} (KBr) 3396, 1656,

1613, 1508; δ_H (270 MHz, $CDCl_3$) 0.85 (3H, t, *J* 7.3, CH_2CH_3), 2.91-3.32 (2H, sym m, CH_2CH_3), 5.38 (1H, br s, one of NH_2), 7.27 (1H, br s, NHEt), 7.29-7.62 (6H, m, ArH, C(3)HN=), 8.45 (1H, br s, one of NH_2); δ_C (67.8 MHz, $CDCl_3$) 14.5 (CH_3, CH_2CH_3), 33.1 (CH_2, CH_2CH_3), 102.4 (C, SC=), 124.8, 128.8, 130.0 (CH, aromatic CH), 144.3 (C, aromatic C), 151.2 [CH, C(3)HN=], 166.4 (C, CO).

Oxygen Nucleophiles

Reaction with lithium methoxide

N-4-Benzyl-3,3-dimethoxy-2-(benzylthio)propanamide 34v and N-4-Benzyl-Z-3-methoxy-2-(benzylthio)propenamide 33v

From a solution of sodium (50 mg, 2.17 mmol) in methanol (10 mL), a 6.4 mL portion was added to a solution of the sulfide **1v** (0.210 g, 0.66 mmol) in methanol (2 mL). After stirring for 1 h the reaction was complete by TLC analysis. Saturated aqueous ammonium chloride (10 mL) and ether (15 mL) were added and the phases were separated, the aqueous layer was extracted with ether (2 × 10 ml) and the combined organic layers were washed with brine (2 × 10 mL), dried and concentrated *in vacuo* to give the crude product (146 mg) as a white solid which was a mixture of mono- and di-substituted products **33v** and **34v** in a ratio of 1:1.8. These were separated by column chromatography on silica gel using hexane:ethyl acetate (60:40) as eluent to give **34v** (36 mg, 16 %) as a white solid, and **33v** (80 mg, 39 %) as a white solid.

34v: ν_{max}/cm^{-1} (KBr) 3282 (br NH), 1644 (CO amide); δ_H (400 MHz, $CDCl_3$) 3.36 [3H, s, one of $(CH_3O)_2$], 3.38 [3H, s, one of $(CH_3O)_2$], 3.41 (1H, d, *J* 4.2, CHS) 3.77 (2H, s, SCH_2Bn), 4.39 (1H, A of ABX, J_{AB} 15.0, J_{AX} 6.0, one of NCH_2Bn), 4.46 (1H, B of ABX, J_{AB} 15.0, J_{BX} 6.0, one of NCH_2Bn), 4.59 [1H, d, *J* 4.2, C(3)H], 6.93 (1H, br t, *J* 5.2, NH), 7.17-7.40 (10H, m, ArH); δ_C (75.5 MHz, $CDCl_3$) 36.5, 43.5 (2 × CH_2, SCH_2 and CH_2NH), 52.4 (CH, CHS), 56.1, 56.6 (2 × CH_3, 2 × OCH_3), 105.4 [CH, C(3)H], 127.35, 127.38, 127.5, 128.62, 128.63, 129.2 (CH, aromatic CH), 137.4, 138.2 (C, aromatic C), 168.9 (C, CO); HRMS (ESI+): Exact mass calculated for $C_{19}H_{24}NO_3S$ ($M+H^+$) 346.1477. Found 346.1466 ($M+H^+$); m/z (ESI^-) 344.1 ($M-H^+$).

33v: ν_{max}/cm^{-1} (KBr) 3379 (br NH), 1648 (CO amide); δ_H (400 MHz, $CDCl_3$) 3.74 (2H, s, SCH_2Bn), 3.89 (3H, s, OCH_3), 4.31 (2H, d, *J* 5.9, NCH_2Bn), 7.00-7.42 (11H, m, ArH, NH),

7.89 (1H, s, C*H*OMe); δ_C (75.5 MHz, $CDCl_3$) 38.9, 43.7 (2 × CH_2, S*C*H_2 and *C*H_2NH), 62.2 (CH_3, O*C*H_3), 102.7 [C, *C*(2)S], 127.24, 127.28, 127.5, 128.5, 128.6, 128.8 (6 × CH, aromatic *C*H), 138.0, 138.3 (C, aromatic *C*), 164.2 (CH, C*H*OCH_3) 165.8 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{18}H_{20}NO_2S$ ($M+H^+$) 314.1215. Found 314.1214 ($M+H^+$); m/z (ESI^+) 314.1 ($M+H^+$).

Formation of β,β-dimethoxyamide

N-*i*-Propyl-3,3-dimethoxy-2-(phenylthio)propanamide 34f

This was prepared following the procedure described for 3,3-dimethoxypropanamide **34a** using **1f** (0.20 g, 0.78 mmol), sodium (38 mg, 1.65 mmol) and methanol (4 and 2 mL). The reaction was complete by TLC analysis after 1 h giving **34f** (0.19 g, 86 %) as a white, crystalline solid which did not require further purification; mp 94−96 °C; (Found C, 58.90; H, 7.68; N, 5.10; S, 11.61. $C_{14}H_{21}NO_3S$ requires C, 59.34; H, 7.47; N, 4.94; S, 11.31%); ν_{max}/cm^{-1} (KBr) 3278 (br NH), 1637 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.06 [3H, d, *J* 7, C(2′)H_3], 1.10 [3H, d, *J* 7, C(2′)H_3], 3.47 (3H, s, OCH_3), 3.50 (3H, s, OCH_3), 3.88 (1H, d, *J* 4, C*H*S), 4.04 (1H, sept, *J* 7, NC*H*), 4.75 [1H, d, *J* 4, C(3)*H*], 6.56 (1H, br d, *J* 7, N*H*), 7.19-7.46 (5H, m, Ar*H*); δ_C (67.8 MHz, $CDCl_3$) 22.3 [*C*(2′)H_3], 41.6 (N*C*H), 56.1, 56.4 (O*C*H_3), 57.1 (*C*HS), 105.1 [*C*(3)H], 127.2, 129.2, 130.8 (aromatic *C*H), 134.2 (aromatic *C*), 167.3 (*C*O); MS *m/z* 283 (M^+, 10 %), 223 (18, M^+-2 x CH_3), 75 (100, $[CH(OMe)_2]^+$).

N-(4-Methylphenyl)-3,3-dimethoxy-2-(*n*-butylthio)propanamide 34r

This was prepared following the procedure described for 3,3-dimethoxypropanamide **34a** using **1r** (0.24 g, 0.86 mmol), sodium (41 mg, 1.81 mmol) and methanol (3 and 3 mL). The reaction was complete after 1 h by TLC analysis. Purification by chromatography using ethyl acetate-hexane (10:90) as eluent gave **34r** (0.20 g, 82%) as a white, crystalline solid; mp 62−64 °C; (Found C, 61.98; H, 8.40; N, 4.80; S, 10.24. $C_{16}H_{25}NO_3S$ requires C, 61.70; H, 8.09; N, 4.50; S, 10.30%); ν_{max}/cm^{-1} (KBr) 3300 (br NH), 1660, 1611 (CO amide); δ_H (270 MHz, $CDCl_3$) 0.89 [3H, t, *J* 7, C(4′)H_3], 1.39-1.44 [2H, m, C(3′)H_2], 1.54-1.62 [2H, m, C(2′)H_2], 2.31 (3H, s, ArCH_3), 2.65 (2H, t, *J* 8, SCH_2), 3.47 (3H, s, OCH_3), 3.53 (3H, s, OCH_3), 3.60 (1H, d, *J* 4, C*H*S), 4.70 [1H, d, *J* 4, C(3)*H*], 7.11-7.45 (4H, ABq, *J* 8, Ar*H*), 8.61 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 13.5 [*C*(4′)H_3], 20.8 (Ar*C*H_3), 21.6 [*C*(3′)H_2], 31.3, 32.1 [*C*(2′)H_2, *C*(1′)H_2], 54.8 (*C*HS), 56.1, 56.8 (2 × O*C*H_3), 105.4 [*C*(3)H], 119.8, 129.4

(aromatic *C*H), 133.9, 135.2 (aromatic *C*), 167.3 (*C*O); MS *m/z* 311 (M^+, 5 %), 251 (8%), 146 (10%), 75 {100%, $[CH(OMe)_2]^+$}.

(1′S)-*N*-(1-Phenylethyl)-3,3-dimethoxy-2-(phenylthio)propanamide 34b

This was prepared following the procedure described for **34a** using **1b** (0.15 g, 0.47 mmol), sodium (23 mg, 0.99 mmol) and methanol (4 mL). After stirring for 2 h the reaction was complete by TLC analysis. Purification by chromatography using ethyl acetate-hexane (25:75) as eluent gave both diastereomers (55:45) of **34b** (145 mg, 89%) as a white, crystalline solid; mp 79−81 °C; $[\alpha]_{20}^{D}$ –57.9 (*c* 4 in ethanol); (Found C, 66.50; H, 6.62; N, 4.40; S, 9.07. $C_{19}H_{23}NO_3S$ requires C, 66.06; H, 6.71; N, 4.06; S, 9.28%); ν_{max}/cm^{-1} (KBr) 3274 (br NH), 1647 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.40, 1.44$^{\diamond}$ [3H, d, *J* 7, C(2′)H_3], 3.40, 3.50$^{\diamond}$ (6H, s, OCH_3), 3.93$^{\diamond}$, 3.95 (1H, d, *J* 2, C*H*S), 4.58, 4.72$^{\diamond}$ [1H, d, *J* 2, C(3)*H*], 5.02-5.13 (1H, m, NC*H*), 7.13-7.42 (10H, m, Ar*H*); δ_C (67.8 MHz, $CDCl_3$) 21.6 [C(2′)H_3], 48.9 (N*C*H), 56.1 (*C*HS), 56.5, 57.1 (O*C*H_3), 105.1 [*C*(3)H], 125.8, 127.2, 128.5, 129.1, 130.9 (aromatic *C*H), 134.0$^{\diamond}$, 134.1, 142.8, 142.9$^{\diamond}$ (aromatic *C*), 167.4 (*C*O); MS *m/z* 345 (M^+, 3%), 225 (18%, M^+-CONHCHCH_3Ph), 107 (43%), 75 {100%, $[CH(OMe)_2]^+$}.

$^{\diamond}$ Major isomer.

3,3-Dimethoxy-2-(phenylthio)propanamide 34k

This was prepared following the procedure described for **34a** using **1k** (0.15 g, 0.7 mmol), sodium (34 mg, 1.47 mmol) and methanol (4 mL) with a reaction time of 16 h, to give **34k** (145 mg, 86%) as a white, crystalline solid which did not require further purification; mp 94−96 °C; ν_{max}/cm^{-1} (KBr) 3375 (br NH), 1655 (CO amide); δ_H (270 MHz, $CDCl_3$) 3.47 (3H, s, OCH_3), 3.52 (3H, s, OCH_3), 3.87 (1H, d, *J* 4, C*H*S), 4.71 [1H, d, *J* 4, C(3)*H*], 5.99 (1H, br s, N*H*), 6.67 (1H, br s, N*H*), 7.14-7.47 (5H, m, Ar*H*); δ_C (67.8 MHz, $CDCl_3$) 56.0 (O*C*H_3), 56.4 (*C*HS), 56.9 (O*C*H_3), 105.0 [*C*(3)H], 127.5, 129.2, 131.0 (aromatic *C*H), 134.1 (aromatic *C*), 171.4 (*C*O); MS *m/z* 241 (M^+, 3%), 209 (M^+-CH_3OH), 110 (47%, PhSH), 75 {100%, $[CH(OMe)_2]^+$}.

***N,N*-Diphenyl-3,3-dimethoxy-2-(phenylthio)propanamide 34n**

This was prepared following the procedure described for **34a** using a mixture of *E* and *Z* isomers (*ca.* 1:1) of **1n** (0.10 g, 0.27 mmol), sodium (13 mg, 0.58 mmol) and methanol (3 mL). The reaction was complete by TLC analysis after 19 h to give pure **34n** (99 mg, 92%) as

a light yellow oil which did not require further purification; (Found C, 69.90; H, 6.07; N, 3.80; S, 8.61. $C_{23}H_{23}NO_3S$ requires C, 70.20; H, 5.89; N, 3.56; S, 8.15%); ν_{max}/cm^{-1} (film) 1668, 1593 (CO amide); δ_H (270 MHz, $CDCl_3$) 3.35 (3H, s, OC*H*$_3$), 3.48 (3H, s, OC*H*$_3$), 4.05 (1H, d, *J* 8, C*H*S), 4.80 [1H, d, *J* 8, C(3)*H*], 7.04-7.37 (15H, m, Ar*H*); δ_C (67.8 MHz, $CDCl_3$) 52.1, 54.9, 57.1 (*C*HS and 2 × O*C*H$_3$), 106.7 [*C*(3)H], 126.2, 126.4, 127.9, 128.2, 128.7, 128.8, 129.4 (aromatic *C*H, 8 signals for 9 carbons), 131.6 (aromatic *C*), 133.4 (aromatic *C*H), 142.1, 142.5 (aromatic *C*), 169.2 (*C*O); MS *m/z* 393 (M^+, 3 %), 333 (18%), 75 {100%, $[CH(OMe)_2]^+$}.

_N_-(4-Methylphenyl)-3,3-dimethoxy-2-(phenylthio)butanamide 34g

This was prepared following the procedure described for **34a** using **1g** (0.13 g, 0.41 mmol), sodium (20 mg, 0.86 mmol) and methanol (6 mL) with a reaction time of 22 h, to give **34g** (128 mg, 91%) as a white, crystalline solid which did not require further purification; mp 97−99 °C; (Found C, 65.64; H, 6.80; N, 4.15. $C_{19}H_{23}NO_3S$ requires C, 66.06; H, 6.71; N, 4.05%); ν_{max}/cm^{-1} (KBr) 3296 (br NH), 1664, 1608 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.71 [3H, s, C(4)*H*$_3$], 2.43 (3H, s, ArC*H*$_3$), 3.44 (3H, s, OC*H*$_3$), 3.50 (3H, s, OC*H*$_3$), 4.22 (1H, s, C*H*S), 7.21-7.61 (9H, m, Ar*H*), 8.43 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 19.4 [*C*(4)H$_3$], 20.8 (Ar*C*H$_3$), 49.4 (*C*HS), 49.9, 60.7 (2 × O*C*H$_3$), 102.0 [*C*(3)], 119.9, 127.4, 129.1, 129.4, 131.1 (aromatic *C*H), 133.9, 134.1, 135.2 (aromatic *C*), 167.1 (*C*O); MS *m/z* 345 (M^+, 5%), 299 (6%, M^+-CH_3, -OCH_3), 89 {79%, $[CCH_3(OMe)_2]^+$}.

Reaction with lithium methoxide

_N_-(2-Propenyl)-3-methoxy-2-(phenylthio)propenamide 33h

This was prepared following the procedure described for **33a** using **1h** (0.20 g, 0.79 mmol), methanol (42 µl, 1.03 mmol), *n*-butyllithium (0.69 mL, 1.6 M in hexane, 1.1 mmol) and THF (4 mL). The reaction was conducted initially at –25 °C, was allowed to warm slowly to room temperature and was complete after a reaction time of 2 h at 0 °C by TLC analysis. Purification by chromatography using ethyl acetate-hexane (30:70) as eluent gave **33h** (135 mg, 69%) as a colourless oil [with < 5% *N*-(2-propenyl)-3,3-dimethoxy-2-(phenylthio)propanamide (estimated by ^{1}H NMR spectroscopic integration)]; ν_{max}/cm^{-1} (film) 3392 (br NH), 1655, 1600; δ_H (270 MHz, $CDCl_3$) 3.85-3.96 (2H, m, NC*H*$_2$), 3.98 (3H, s, OC*H*$_3$), 4.93-5.04 (2H, m, C*H*$_2$=), 5.68-5.82 (1H, m, C*H*=), 7.00 (1H, br s, N*H*), 7.11-7.29 (5H, m, Ar*H*), 8.11 (1H, s, C*H*=); δ_C (67.8 MHz, $CDCl_3$) 41.9 (N*C*H$_2$), 62.4 (*C*H$_3$O), 101.2

(S*C*=), 115.7 (*C*H_2=), 125.8, 126.3, 128.8, (aromatic *C*H), 133.8 (*C*H=), 135.4 (aromatic *C*), 165.2 (*C*O), 165.6 (=*C*HO); MS *m/z* 249 (M^+, 100 %), 234 (2%, M^+-CH_3), 218 (8%, M^+-OCH_3), 193 (21%, M^+-$NHCH_2CH{=}CH_2$), 165 (18%, M^+-$CONHCH_2CH{=}CH_2$).

_N,N_-Diphenyl-3-methoxy-2-(phenylthio)propenamide 33n

This was prepared following the procedure described for **33a** using an *E* and *Z* mixture (*ca.* 1:1) of isomers of **1n** (0.20 g, 0.55 mmol), methanol (29 μl, 0.72 mmol), *n*-butyllithium (0.48 mL, 1.6 M in hexane, 0.77 mmol) and THF (4 mL) with a reaction time of 18 h while warming slowly from –78 °C to room temperature to give a brown oil (0.23 g) which was a mixture of compounds. Purification by chromatography using ethyl acetate-hexane (25:75) as eluent gave **34n** (62 mg, 31%) and **33n** (22 mg, 11%, containing **34n** in ratio of 4:1) as a yellow oil; ν_{max}/cm^{-1} (film) 1670, 1593 (CO amide); δ_H (270 MHz, $CDCl_3$) 3.74 (3H, s, OC*H*$_3$), 6.51 (1H, s, C*H*=), 6.86-7.46 (15H, m, Ar*H*); δ_C (67.8 MHz, $CDCl_3$) 61.3 (O*C*H_3), 105.8 (S*C*=), 125.8, 126.5, 127.8, 127.2, 128.7, 127.9, 128.6, 128.8, 129.0 (aromatic *C*H), 133.4, 136.9, 142.7 (aromatic *C*), 158.1 (*C*H=), 166.7 (*C*O); MS *m/z* (as a mixture with acetal **33n**) 361 (M^+, 30%), 333 (20%), 252 (27%, M^+-SPh), 193 (54%, M^+-NPh_2).

***N*-(4-Methylphenyl)-3-methoxy-2-(*n*-butylthio)propenamide 33r**

This was prepared following the procedure described for **33a** using **1r** (0.20 g, 0.71 mmol), methanol (37 μl, 0.92 mmol), *n*-butyllithium (0.62 mL, 1.6 M in hexane, 0.99 mmol) and THF (4 mL). Addition of the methoxide solution was conducted when both solutions were at –23 °C. After stirring for 4 h, allowing the reaction to warm slowly to 10 °C, the reaction was complete by TLC analysis. Purification by chromatography using ethyl acetate-hexane (25:75) as eluent gave **34r** (12 mg, 5%) and **33r** (58 mg, 30%) (as a mixture with < 30% **34r**) as a yellow oil. ν_{max}/cm^{-1} (film) 3331 (br NH), 1666, 1603 (CO amide); δ_H (270 MHz, $CDCl_3$) 0.90 [3H, t, *J* 7, C(4′)*H*$_3$], 1.34-1.51 [2H, m, C(3′)*H*$_2$], 1.52-1.68 [2H, m, C(2′)*H*$_2$], 2.32 (3H, s, ArC*H*$_3$), 2.64 (2H, t, *J* 7, SC*H*$_2$), 3.95 (3H, s, OC*H*$_3$), 7.13-7.50 (4H, ABq, *J* 8, Ar*H*), 7.94 (1H, s, C*H*=), 9.03 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 13.6 [*C*(4′)H_3], 20.8 (Ar*C*H_3), 21.9 [*C*(3′)H_3], 31.5 [*C*(2′)H_2], 34.7 [*C*(1′)H_2], 62.2 (O*C*H_3), 104.0 (S*C*=), 119.7, 129.4 (aromatic *C*H), 133.6, 135.6 (aromatic *C*), 163.0 (*C*O), 164.1 (*C*H=); MS *m/z* 279 (M^+, 73%), 173 (37%, M^+-NH*p*Tol), 107 (57%), 75 (100%).

***N*-(4-Methylphenyl)-3-methoxy-2-(phenylthio)-2-butenamide 33g**

This was prepared following the procedure described for **33a** using an *E* and *Z* mixture (*ca.*1:1) of isomers of **1g** (0.20 g, 0.63 mmol), methanol (33 μl, 0.82 mmol), *n*-butyllithium (0.55 mL, 1.6 M in hexane, 0.88 mmol) and THF (5 mL) with a reaction time of 18 h while warming slowly from −78 °C to room temperature. Purification by chromatography using ethyl acetate-hexane (20:80) as eluent gave unreacted **1g** (35 mg, 18 %) (spectroscopic characteristics as described above) and a fraction containing the *E* and *Z* isomers of **33g** (ratio 1:5) as an inseparable mixture with **34g** (ratio 50:50) (104 mg); ν_{max}/cm^{-1} (film) 3345 (br NH), 1651, 1592 (CO α,β-unsaturated amide); δ_H (270 MHz, $CDCl_3$) signals assigned to *E/Z* isomers at 2.46, 2.73 [C(4)H_3], 3.82, 3.94 (OCH_3) others are indistinguishable.

Reaction with sodium ethoxide

N-(4-Benzyl)-*Z*-3-ethoxy-2(benzylthio)propenamide 35v and *N*-(4-Benzyl)-3,3-diethoxy-2(benzylthio)propenamide 36v

1v (0.30 g, 0.94 mmol) was added in one portion to a freshly prepared solution of sodium ethoxide [sodium (44 mg, 1.88 mmol) in ethanol (12 mL)] at 0˚C and left to stir for 1 h. The reaction mixture was quenched with saturated aqueous ammonium chloride (15 mL) and ether (15 mL). The phases were separated and the aqueous layer was extracted with ether (2 × 10 mL). The combined organic layers were then washed with brine (2 × 10 ml), dried and evaporated to give the crude product (302 mg) as an off white solid which was a mixture of mono- and di-substituted products **35v** and **36v** in a ratio of 1:1.2. These were separated by column chromatography on silica gel using hexane:ethyl acetate (60:40) as eluent to give the disubstituted product **36v** (0.12 g, 34%) as a white solid, and the monosubstituted **35v** (0.101 g, 32%) as a yellow oil.

35v: ν_{max}/cm^{-1} (KBr) 3389 (br NH), 1648 (CO amide); δ_H (400 MHz, $CDCl_3$) 1.33 (3H, t, *J* 7.1, CH_3CH$_2$O), 3.74 (2H, s, SCH_2Bn), 4.13 (2H, q, *J* 7.1, CH$_3$CH_2O), 4.32 (2H, d, *J* 5.9, NCH_2Bn), 7.05-7.39 (11H, m, Ar*H,* N*H*), 7.97 (1H, s, C*H*OEt); δ_C (75.5 MHz, $CDCl_3$) 15.5 (CH$_3$, OCH$_2$*C*H$_3$), 38.8, 43.6 (2 × CH$_2$, S*C*H$_2$ and *C*H$_2$NH), 71.1 (CH$_2$, O*C*H$_2$CH$_3$), 102.3 [C, *C*(2)S], 127.2, 127.3, 127.5, 128.5, 128.6, 128.8 (6 × CH, aromatic *C*H), 138.1, 138.4 (2 × C, aromatic *C*), 163.0 (CH, C*H*OCH$_2$CH$_3$) 166.0 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{19}H_{22}NO_2S$ ($M+H^+$) 328.1371. Found 328.1356 ($M+H^+$); m/z (ESI^+) 328.1 ($M+H^+$).

36v: ν_{max}/cm^{-1} (KBr) 3282 (br NH), 1644 (CO amide); δ_H (400 MHz, $CDCl_3$) 1.14 [3H, t, *J* 5.1, one of (CH_3CH$_2$O)$_2$], 1.16 [3H, t, *J* 5.1, one of (CH_3CH$_2$O)$_2$], 3.37 (1H, d, *J* 4.1, C*H*S), 3.38-3.53 (2H, m, one of CH_2CH$_3$O), 3.60-3.72 (2H, m, one of CH_2CH$_3$O), 3.77 (1H, A of

AB system, J_{AB} 13.6, one of SCH_2Bn), 3.81 (1H, B of AB system, J_{AB} 13.6, one of SCH_2Bn), 4.38 (1H, A of ABX, J_{AB} 15.2, J_{AX} 5.6, one of NCH_2Bn), 4.49 (1H, B of ABX, J_{AB} 15.2, J_{BX} 5.6, one of NCH_2Bn), 4.73 [1H, d, *J* 4.1, C(3)*H*], 7.00 (1H, br t, *J* 5.2, N*H*), 7.19-7.37 (10H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 15.1 (CH_3, 2 × OCH_2CH_3), 36.5 (2 × CH_2, SCH_2 and CH_2NH), 52.9 (CH, *C*HS), 64.2, 64.7 (2 × CH_2, OCH_2CH_3), 103.0 [CH, *C*(3)H], 127.3, 127.4, 128.6, 129.2 (4 × CH, aromatic *C*H), 137.6, 138.2 (2 × C, aromatic *C*), 169.3 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{21}H_{28}NO_3S$ ($M+H^+$) 374.1790. Found 374.1783 ($M+H^+$); m/z (ESI^+) 374.2 ($M+H^+$).

Reaction of alkoxides with sulfoxides

N-(4-Methylphenyl)-3,3-dimethoxy-2-(phenylsulfinyl)propanamide 37a

From a solution of sodium (50 mg, 2.17 mmol) in methanol (10 mL), a 6.4 mL portion was added to a solution of **18a** (0.21 g, 0.66 mmol) in methanol (4 mL). After stirring for 1 h the reaction was complete (by TLC analysis). Saturated aqueous ammonium chloride (10 mL) and ether (15 mL) were added and the phases were separated, the aqueous layer was extracted with ether (2 × 10 mL) and the combined organic layers were washed with brine (2 × 10 mL), dried and evaporated to give the crude product **37a** (194 mg, 85%) as a white solid which was a 1.8:1 mixture of diastereomers. These diastereomers were separated by column chromatography on silica gel using hexane:ethyl acetate (60:40) as eluent.

Major diastereomer: (129 mg, 56%); ν_{max}/cm^{-1} (KBr) 3301 (br NH), 1677 (CO amide), 1072 (SO); δ_H (400 MHz, $CDCl_3$) 2.29 (3H, s, ArCH_3), 3.46 (3H, s, one of OCH_3), 3.60 [1H, d, *J* 8.0, C*H*S(O)], 3.61 (3H, s, one of OCH_3), 5.08 [1H, d, *J* 8.0, C(3)*H*], 7.08 (2H, d, *J* 8.4, Ar*H*), 7.28 (2H, d, *J* 8.4, Ar*H*), 7.39-7.48 (3H, m, Ar*H*), 7.52-7.61 (2H, m, Ar*H*), 8.97 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 20.9 (CH_3, ArCH_3), 53.3, 55.7 (2 × CH_3, 2 × OCH_3), 69.7 (CH, *C*HS), 101.2 [CH, *C*(3)H], 120.5, 124.1, 129.4, 131.6 (4 × CH, aromatic *C*H), 134.2, 134.8, 139.4 (3 × C, aromatic *C*), 161.4 (C, *C*O) HRMS (ESI+): Exact mass calculated for $C_{17}H_{18}NO_3S$ ($M-CH_3O^-$) 316.1007. Found 316.1014 ($M-CH_3O^-$); m/z (ESI^+) 348.1 ($M+H^+$), 316.0 ($M-CH_3O^-$).

Minor diastereomer: (62 mg, 27%); ν_{max}/cm^{-1} (KBr) 3282 (br NH), 1681, 1599 (CO amide), 1070 (SO); δ_H (400 MHz, $CDCl_3$) 2.31 (3H, s, ArCH_3), 3.50 (3H, s, one of OCH_3), 3.59 (3H, s, one of OCH_3), 4.01 [1H, d, *J* 6.0, C*H*S(O)], 4.78 [1H, d, *J* 6.0, C(3)*H*], 7.10 (2H, d, *J* 8.4, Ar*H*), 7.31 (2H, d, *J* 8.4, Ar*H*), 7.43-7.54 (3H, m, Ar*H*), 7.62-7.68 (2H, m, Ar*H*), 8.45 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 20.9 (CH_3, ArCH_3), 54.3, 57.2 (2 × CH_3, OCH_3),

71.6 (CH, *C*HS), 101.5 [CH, *C*(3)H], 120.2, 125.2, 129.2, 129.4, 132.1 (5 × CH, aromatic *C*H), 134.2, 134.8, 140.1 (3 × C, aromatic *C*), 161.0 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{17}H_{18}NO_3S$ (M-CH_3O^-) 316.1007. Found 316.1006 (M-CH_3O^-); m/z (ESI^+) 348.0 (M+H^+), 316.0 (M-CH_3O^-).

***N*-4-Benzyl-*3*,3-dimethoxy-2-(benzylsulfinyl)propanamide 37g**

From a solution of sodium (50 mg, 2.17 mmol) in methanol (10 mL) a 6.4 ml portion was added to a solution of **18g** (0.22 g, 0.66 mmol) in methanol (4 mL). After stirring for 1 h the reaction was complete by TLC analysis. Saturated aqueous ammonium chloride (10 mL) and ether (15 mL) were added and the phases were separated, the aqueous layer was extracted with ether (2 × 10 mL) and the combined organic layers were washed with brine (2 × 10 mL), dried and concentrated *in vacuo* to give the crude product (130 mg) as a white solid. Purification by column chromatography on silica gel using hexane:ethyl acetate (40-60 % ethyl acetate gradient) as eluent gave the pure major diastereomer as a white solid (99 mg, 42%). A second fraction was isolated containing a 1.72:1 diastereomeric mixture of the major and minor diastereomers, white solid (26 mg).

Major diastereomer: ν_{max}/cm^{-1} (KBr) 3297 (br NH), 1656, 1535 (CO amide), 1071 (SO); δ_H (400 MHz, $CDCl_3$) 3.37 (3H, s, one of OC*H*$_3$), 3.40 (3H, s, one of OC*H*$_3$), 3.47 [1H, d, *J* 7.8, C*H*S(O)], 3.99 (1H, A of ABq, *J* 12.8, one of SCH_2), 4.05 (1H, B of AB system, *J* 12.8, one of SCH_2), 4.57 (2H, d, *J* 6.0, NC*H*$_2$Bn), 4.91 [1H, d, *J* 7.8, C(3)*H*], 7.22-7.42 (10H, m, Ar*H*), 7.55 (1H, br t, *J* 5.6, N*H*); δ_C (75.5 MHz, $CDCl_3$) 43.6 (CH_2, *C*H_2NH), 53.6 (CH_3, one of OCH_3), 55.3 (CH_3, one of OCH_3), 56.4 (CH_2, S*C*H_2), 63.3 (CH, *C*HS), 101.3 [CH, *C*(3)H], 127.5, 127.9, 128.66, 128.72, 129.1, 130.4 (CH, aromatic *C*H), 129.0, 138.0 (C, aromatic *C*), 164.3 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{19}H_{24}NO_4S$ (M+H^+) 362.1426. Found 362.1419 (M+H^+); m/z (ESI^+) 362.1 (M+H^+).

Characteristic signals for the **minor diastereomer:** δ_H (400 MHz, $CDCl_3$) 3.42 (1H,s, one of OCH_3), 3.57 (1H, s, one of OCH_3), 3.77 (1H, d, *J* 4.0, C*H*S), 3.98 (1H, A of ABq, *J* 12.9, one of SCH_2), 4.25 (1H, B of AB system, *J* 12.9, one of SCH_2), 4.52 [2H, d, *J* 5.9, C(3)*H*], 4.80 [1H, d, *J* 4.0, CH$(OMe)_2$]; δ_C (75.5 MHz, $CDCl_3$) 43.5 (CH_2, *C*H_2NH), 56.3, 56.7 (2 × CH_3, 2 × OCH_3), 57.6 (CH_2, S*C*H_2) 66.7 (CH, *C*HS), 102.4 [CH, *C*(3)H], 127.5, 128.4, 128.8, 130.7 (CH, aromatic *C*H), 129.8, 137.8 (C, aromatic *C*), 164.4 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{19}H_{24}NO_4S$ (M+H^+) 362.1426. Found 362.1429 (M+H^+); m/z (ESI^+) 362.1 (M+H^+).

_N_-(4-Methylphenyl)-3,3-diethoxy-2-(phenylsulfinyl)propanamide 38a

From a solution of sodium (100 mg, 4.34 mmol) in ethanol (20 mL), a 12.8 mL portion was added to a solution of **18a** (0.421 g, 1.32 mmol) in ethanol (8 mL). After stirring for 1 h the reaction was complete (by TLC analysis). Saturated aqueous ammonium chloride (10 mL) and ether (15 mL) were added and the phases were separated, the aqueous layer was extracted with ether (2 × 10 mL) and the combined organic layers were washed with brine (2 × 10 mL), dried and evaporated to give the crude product **38a** (327 mg, 66%) as a white solid which was a 2:1 mixture of diastereomers. Following purification by column chromatography on silica gel using hexane:ethyl acetate (60:40) as eluent, the major diastereomer was obtained as a white solid (218 mg, 44%). A second fraction was isolated containing a 1:1.4 diastereomeric mixture of the major and minor diastereomers, white solid (99 mg).

Major diastereomer: ν_{max}/cm^{-1} (KBr) 3308 (NH), 1666 (CO amide), 1514, 1059 (S-O); δ_H (400 MHz, $CDCl_3$) 1.20 (3H, t, *J* 7.0, OCH_2CH_3), 1.35 (3H, t, *J* 7.0, OCH_2CH_3), 2.30 (3H, s, $ArCH_3$), 3.59 [1H, d, *J* 7.8, *CH*S(O)], 3.62-3.98 (4H, m, 2 × OCH_2CH_3), 5.19 [1H, d, *J* 7.8, C(3)*H*], 7.08 (2H, d, *J* 8.4, Ar*H*), 7.27 (2H, d, *J* 8.4, Ar*H*), 7.41-7.49 (3H, m, Ar*H*), 7.53-7.61 (2H, m, Ar*H*), 8.96 (1H, bs, N*H*); δ_C (75.5 MHz, $CDCl_3$) 15.1 (CH_3, 2 × OCH_2CH_3), 20.9 (CH_3, $ArCH_3$), 62.1, 64.3 (2 × CH_2, OCH_2CH_3), 70.5 (CH, *C*HS), 99.5 [CH, *C*(3)H], 120.5, 124.1, 129.4, 131.5 (4 × CH, aromatic *C*H), 134.1, 134.9, 139.6 (3 × C, aromatic C), 161.6 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{18}H_{20}NO_3S$ (M-$CH_3CH_2O^-$) 330.1164. Found 330.1172 (M-$CH_3CH_2O^-$); m/z (ESI^+) 374.1 (M+H^+), 330.0 (M-$CH_3CH_2O^-$).

The stereochemistry was determined by single crystal X-ray diffraction on a crystalline sample of **38a** recrystallised from acetonitrile/acetone. Crystals of **38a** are orthorhombic, space group $P\text{-}2_12_12_1$, formula $C_{20}H_{25}NO_4S$, M = 375.47, a = 5.3188(18) Å, b = 12.594(4) Å, c = 29.209(10) Å, U = 1956.6(12) $Å^3$, F(000) = 800, μ(Mo-Kα) = 0.190 mm^{-1}, $R(F_o)$ = 0.0738, for 3455 observed reflections with $I>2\sigma(I)$, $wR_2(F^2)$ = 0.1344 for all 1716 unique reflections. Data in the θ range 1.39-25.03 ° were collected at 150 K on a Bruker Apex II Duo diffractometer using Mo-Kα graphite monochromated radiation, λ = 0.7107 Å, and corrected for Lorentz and polarization effects. The structure was solved by direct methods and refined by full-matrix least-squares using all F^2 data. The hydrogen atoms were placed in calculated positions and allowed to ride on the parent atom.

Characteristic signals for the **minor diastereomer:** Characteristic signals due to the minor diastereomer: ν_{max}/cm^{-1} (KBr) 3308 (NH), 1666 (CO amide), 1514, 1059 (SO); δ_H (400 MHz, $CDCl_3$) 1.26 (3H, t, *J* 7.0, OCH_2CH_3), 1.30 (3H, t, *J* 7.0, OCH_2CH_3), 2.30 (3H, s, $ArCH_3$), 3.98 [1H, d, *J* 5.4, C*H*S(O)], 4.98 [1H, d, *J* 5.4, C(3)*H*], 8.63 (1H, bs, N*H*).

***N*-Benzyl-3-3-diethoxy-2-(benzylsulfinyl)propenamide 38g**

18g (0.30 g, 0.94 mmol) was added in one portion to a freshly prepared solution of sodium ethoxide [sodium (41 mg, 1.8 mmol) in ethanol (12 mL)] at 0˚C and stirred for 1 hour. The reaction mixture was then quenched with saturated aqueous ammonium chloride (15 mL) and ether (15 ml). The phases were separated and the aqueous layer extracted with ether (2 × 10 mL). The combined organic layers were washed with brine (2 × 10 mL), dried and evaporated to give the crude product (0.38 g) as a yellow solid and a 1.1:1 mixture of diastereomers. This was purified by column chromatography on silica gel using hexane:ethyl acetate as eluent (20-40% ethyl acetate gradient elution) to give the pure product as an off-white solid (0.32 g, 90%), as a 2.9:1 diastereomeric mixture; ν_{max}/cm^{-1} (KBr) 3415 (NH), 1655 (CO amide), 1064 (SO);

Major diastereomer: δ_H (400 MHz, $CDCl_3$) 1.16 (3H, t, *J* 6.8, one of OCH_2CH_3), 1.19 (3H, t, *J* 6.8, one of OCH_2CH_3), 3.46-3.77 [5H, m, 2 × OCH_2CH_3 and C*H*S(O); CHS(O) could be seen as a doublet at 3.49, *J* 7.6], 3.99 (1H, A of AB system, *J* 12.8, one of SCH_2), 4.07 (1H, B of AB system, *J* 12.8, one of SCH_2), 4.49-4.64 (2H, m, NCH_2Bn), 5.03 [1H, d, *J* 7.6, C(3)*H*], 7.22-7.41(10H, m, Ar*H*), 7.48 (1H, br t, N*H*); δ_C (75.5 MHz, $CDCl_3$) 15.0, 15.1 (2 × CH_3, 2 × OCH_2CH_3), 43.5 (CH_2, CH_2NH), 56.5 (CH_2, SCH_2), 62.3, 64.0 (2 × CH_2, 2 × OCH_2CH_3), 64.4 (CH, *C*HS), 99.6 [CH, *C*(3)H], 127.5, 127.9, 128.6, 128.7, 129.1, 130.4 (6 × CH, aromatic *C*H), 136.8, 138.5 (2 × C, aromatic *C*), 164.5 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{21}H_{28}NO_4S$ ($M+H^+$) 390.1739. Found 390.1732 ($M+H^+$).

Characteristic signals due to the **minor diastereomer**: δ_H (400 MHz, $CDCl_3$) 1.18 (3H, t, *J* 6.8, one of OCH_2CH_3), 1.21 (3H, t, *J* 6.8, one of OCH_2CH_3), 3.99 (1H, A of AB system, *J* 13.2, one of SCH_2), 4.30 (1H, B of AB system, *J* 13.2, one of SCH_2), 4.96 [1H, d, *J* 3.7, C(3)*H*].

Addition of ethylene glycol

2-[*N*-Benzyl-(2-phenylthio)-acetamide]-1,3-dioxolane 39c

Ethylene glycol (0.1 mL, 2.07 mmol) was dissolved in THF (7 mL) and cooled to 0 °C. *n*-Butyllithium (1.6 M solution in hexanes, 1.2 mL, 1.98 mmol) was added, and the solution stirred

at 0 °C for 10 min, and subsequently warmed to room temperature. A solution of **1c** (0.30 g, 0.99 mmol) in THF (7 mL) was added and the reaction mixture stirred for 18 h, at which point TLC showed the reaction to be complete. A saturated aqueous ammonium chloride solution (40 mL) and CH_2Cl_2 (40 mL) were added and the layers separated. The aqueous layer was washed with CH_2Cl_2 (2 × 40 mL) and the combined organic layers were washed with brine (40 mL). The solution was then dried over $MgSO_4$ and the solvent evaporated at reduced pressure to give the crude product. This was purified by column chromatography on silica gel using ethyl acetate/hexane (30:70) as eluent, to give **36c** as a white crystalline solid (0.16 g, 50%); mp 86−88 °C; (Found C, 65.52; H, 5.82; N, 4.16; S, 9.95; $C_{18}H_{19}NO_3S$ requires C, 65.63; H, 5.81; N, 4.25; S, 9.73%); ν_{max}/cm^{-1} (KBr) 3314 (NH), 2923 (CH), 1655 (CO), 1522 (C=C); δ_H (270 MHz, $CDCl_3$) 3.85-4.01 [5H, m, C(4)H_2, C(5)H_2, C*H*SPh], 4.36-4.55 (2H, sym m, NCH_2Ph), 5.45 (1H, d, *J* 2.7, O_2C*H*), 7.14-7.43 (11H, m, N*H*, Ar*H*); δ_C (67.8 MHz, $CDCl_3$) 43.8 (N*C*H_2Ph), 58.0 (*C*HSPh), 65.8, 66.0 [O*C*(4)H_2 and O*C*(5)H_2], 103.1 (O_2*C*H), 127.2, 127.6, 128.6, 129.2, 130.9 (aromatic *C*H), 134.0, 138.0 (aromatic *C*), 167.8 (*C*O); MS *m/z* 329 (M^+, 9%), 91 [84%, $(CH_2Ph)^+$], 73 [100%, $(CHO_2C_2H_4)^+$].

2-[*N*-(4-Methylphenyl)-(2-phenylsulfinyl)acetamide]-1,3-dioxolane 40a

n-Butyllithium (0.99 mL, 1.56 mmol) was added to a solution of ethylene glycol (102 μL, 1.65 mmol) in anhydrous THF at 0˚C. The solution was left stir for 20 min, removed from the ice bath and left warm to room temperature over ten minutes. A solution of **18a** (0.25 g, 0.78 mmol) in anhydrous THF (6 mL) was added rapidly to the reaction mixture. After stirring for 16 h the reaction was complete (by TLC analysis) and saturated aqueous ammonium chloride (30 mL) and dichloromethane (30 mL) were added. The phases were separated, the aqueous phase extracted with dichloromethane (2 × 30 mL), the combined organic layers were then washed with brine (2 × 60 mL) dried and concentrated *in vacuo* to give the crude acetal 1.2:1 diastereomeric mixture. This was purified by column chromatography on silica gel using hexane:ethyl acetate (60:40) as eluent to give the pure acetal **40a** as a yellow solid (180 mg, 67%), and as a 3.1:1 diastereomeric mixture.

ν_{max}/cm^{-1} (KBr) 3298 (NH), 1670 (CO amide), 1035 (SO); HRMS (ESI+): Exact mass calculated for $C_{18}H_{20}NO_4S$ ($M+H^+$) 346.4136. Found 346.1101 ($M+H^+$); m/z (ESI^+) 346.1 ($M+H^+$).

Major diastereomer: δ_H (400 MHz, $CDCl_3$) 2.30 (3H, s, ArCH_3), 3.48 [1H, d, *J* 4.6, C*H*S(O)], 4.05-4.15 (2H, m, OCH_2), 3.98-4.27 (2H, m, OCH_2), 5.62 [1H, d, *J* 4.6, C(3)*H*],

7.06-7.79 (9H, m, Ar*H*), 9.23 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 20.9 (CH_3, Ar*C*H_3), 65.9 (CH_2, 2 × *C*H_2O), 70.4 (CH, *C*HS), 101.5 [CH, *C*(3)H], 120.5, 124.1, 129.4, 129.5, 131.7 (5 × CH, aromatic *C*H), 134.4, 134.8, 139.8 (3 × C, aromatic *C*), 161.0 (C, *C*O);

Minor diastereomer: Characteristic signals due to the minor diastereomer: δ_H (400 MHz, $CDCl_3$) 3.95 [1H, d, *J* 5.27, C*H*S(O)], 5.30 [1H, d, *J* 5.27, C(3)*H*], 8.41 (1H, br s, N*H*).

Addition of chiral diols

(4*S*,5*S*)-4,5-Dimethyl-2-[*N*-(4-methylphenyl)-(2-phenylthio)acetamide]-1,3-dioxolane 43a

This was prepared following the procedure described for **42a** using **1a** (0.15 g, 0.5 mmol), (2*S*, 3*S*)-2,3-butanediol **41b** (94 mg, 1.04 mmol), *n*-butyllithium (0.62 mL, 1.6 M in hexane, 0.99 mmol) and THF (6 mL). The reaction was complete by TLC analysis after stirring at room temperature for 1.5 h. Purification by chromatography using ethyl acetate-hexane (25:75) as eluent gave **43a** (75 mg, 43%) (as a 53:47 mixture of diastereomers) as a white, crystalline solid; mp 74−76 °C; $[\alpha]_{20}^{D}$+15.4 (*c* 7 in ethanol); (Found C, 67.08; H, 6.50; N, 3.80; S, 9.22. $C_{20}H_{23}NO_3S$ requires C, 67.20; H, 6.49; N, 3.92; S, 9.87%); ν_{max}/cm^{-1} (film) 3311 (NH), 1660, 1604 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.26, 1.29 [3H, d, *J* 6, C*H*$_3$C(4) or C*H*$_3$C(5)], 1.34, 1.38 [3H, d, *J* 6, C*H*$_3$C(4) or C*H*$_3$C(5)], 2.32 (3H, s, ArC*H*$_3$), 3.69-3.90 [2H, m, C(4)*H* and C(5)*H*], 4.08, 4.09 (1H, d, *J* 2, C*H*S), 5.50, 5.65 [1H, d, *J* 2, C(2)*H*], 7.11-7.49 (9H, m, Ar*H*), 8.57, 8.64 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 16.2, 16.4, 16.88, 16.91 [*C*H$_3$C(4) and *C*H$_3$C(5)], 20.8 (Ar*C*H$_3$), 58.5, 59.3 (*C*HS), 79.4, 79.7, 80.3, 80.5 [*C*(4)H and *C*(5)H], 101.7, 101.9 [*C*(2)H], 119.6, 119.7, 127.4, 127.5, 129.20, 129.24, 130.7, 131.0 (aromatic *C*H), 133.6, 133.8, 134.0, 134.1, 135.0, 135.1 (aromatic *C*), 166.0, 166.1 (*C*O); MS *m/z* 357 (M^+, 10%), 317 (2%), 101 [100%, $(C_5H_9O_2)^+$], 73 (50%).

(4*R*,6*R*)-4,6-Dimethyl-2-[*N*-(4-phenylmethyl)-2-(phenylthio)acetamide]-1,3-dioxane 44a

This was prepared following the procedure described for the preparation of **42a** using **1a** (0.20 g, 0.66 mmol), (2*R*, 4*R*)-2,4-pentanediol **41c** (144 mg, 1.39 mmol), *n*-butyllithium (0.83 mL, 1.6 M in hexane, 1.32 mmol) and THF (6 mL). The reaction was complete by TLC analysis after stirring at room temperature for 5 min. Purification by chromatography using ethyl acetate-hexane (15:85) as eluent gave **44a** (128 mg, 52%) (as a 1:1 mixture of diastereomers) as a colourless oil; $[\alpha]_{20}^{D}$ –7.7 (*c* 10 in ethanol); ν_{max}/cm^{-1} (film) 3332 (br NH), 1686, 1602 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.21, 1.28 [3H, d, *J* 7, C*H*$_3$C(4) or C*H*$_3$C(6)], 1.31, 1.38 [3H, d, *J* 7, C*H*$_3$C(4) or C*H*$_3$C(6)], 1.77 [1H, br s, C(5)H_AH_B], 1.82-1.96

[1H, ddd, *J* 25, 13, 3, C(5)H$_A$*H$_B$*], 2.30 (3H, s, ArC*H*$_3$), 3.92, 3.95 (1H, d, *J* 3, C*H*S), 3.93-4.17, 4.34-4.52 [2H, m, C(4)*H* and C(6)*H*], 5.40 [1H, d, *J* 3, C(2)*H*], 7.03-7.49 (9H, m, Ar*H*), 8.64, 8.69 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 16.9, 20.8, 21.5, 21.7 [*C*H$_3$C(4), *C*H$_3$C(6) and Ar*C*H$_3$], 36.4, 36.6 [*C*(5)H$_2$], 57.9, 58.2 (*C*HS), 68.2, 68.7, 69.0 [*C*(4)H and *C*(6)H], 93.1, 93.3 [*C*(2)H], 119.8, 120.0 (aromatic *C*H), 125.5 (aromatic *C*), 127.2, 128.8, 129.3, 130.8, (aromatic *C*H), 130.9, 133.8, 134.1, 134.3, 135.2, 138.0 (aromatic *C*), 166.5, 166.6 (*C*O); MS *m/z* 371 (M^+, 50%), 263 (15%), 177 (13%), 115 [100%, $(C_6H_{11}O_2)^+$], 91 (35%); Found (HRMS, EI) M^+ 371.15052 $C_{21}H_{25}NO_3S$ *m/z* 371.15552.

(4*R*,5*R*)-4,5-Di(ethoxycarbonyl)-2-[*N*-(4-phenylmethyl)-2-(phenylthio)acetamide]-1,3-dioxolane 45a

n-Butyllithium (0.83 mL, 1.6 M in hexane, 1.32 mL) was added to a solution of DIPA (188 µl, 1.35 mmol) in THF (3 mL) at 0 °C. After stirring for 15 min, (2*R*, 3*R*)-diethyl tartrate **41d** (0.29 g, 1.39 mmol) was added and stirring was continued at 0 °C for a further 10 min. A solution of **1a** (0.20 g, 0.66 mmol) in THF (3 mL) at 0 °C was added dropwise. After stirring for 1 h the reaction was complete by TLC analysis and saturated aqueous ammonium chloride (10 mL) and ether (20 mL) were added. The phases were separated, ether (2 × 10 mL) was used to extract the aqueous phase and the combined organic layers were washed with brine (3 × 10 mL), dried and evaporated to give the crude dioxolane **45a** (0.26 g, 82%). Purification by chromatography using ethyl acetate-hexane (50:50) as eluent gave **45a** (0.21 g, 66%) (as a 58:42 mixture of diastereomers) as an off-white, crystalline solid; mp 85−87 °C; $[\alpha]_{20}^{D}$ −10.1 (*c* 10 in CH_2Cl_2); ν_{max}/cm^{-1} (KBr) 3476 (NH), 1746 (CO ester), 1668 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.20-1.45 (6H, 2 × m, 2 × C*H*$_3$CH$_2$O), 2.30 (3H, s, ArC*H*$_3$), 4.05 (*ca.* 0.5H, d, *J* 5, C*H*S for one diasteromer), 4.18-4.32 (4.5H, m, OC*H*$_2$ and C*H*S of other diastereomer), 4.75-5.05 [2H, m, C(4)*H* and C(5)*H*], 5.77$^{\diamond}$, 5.87 [1H, d, *J* 4, C(2)*H*], 7.09-7.56 (9H, m, Ar*H*), 8.59 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 14.0 (*C*H$_3$CH$_2$O), 20.8 (Ar*C*H$_3$), 57.3$^{\diamond}$, 58.1 (*C*HS), 62.1$^{\diamond}$, 62.4 (O*C*H$_2$), signals for *C*(4)H and *C*(5)H were obscured by $CDCl_3$ at 76-78 ppm, 105.5, 106.0$^{\diamond}$ [*C*(2)H], 119.7, 127.5, 129.3, 131.8, 132.4 (aromatic *C*H), 132.8, 133.1, 133.9, 134.2, 134.8, 135.1 (aromatic *C*), 164.9, 165.4, 168.2, 168.64 168.9, 169.1 (*C*O amide and ester); MS *m/z* 473 (M^+, 1 %), 216 (100), 106 (47); Found (HRMS, EI) M^+ 473.14898 $C_{24}H_{27}NO_7S$ requires *m/z* 473.15083.

$^{\diamond}$ Major isomer.

(4*R*,5*R*)-4,5-Dimethyl-2-[(S)-*N*-(1-phenylethyl)-2-(phenylthio)acetamide]-1,3-dioxolane 42b

This was prepared following the procedure described for **42a** using **1b** (0.20 g, 0.63 mmol), (2*R*, 3*R*)-2,3-butanediol **41a** (119 mg, 1.32 mmol), *n*-butyllithium (0.79 mL, 1.6 M in hexane, 1.26 mmol) and THF (6 mL). The reaction was complete by TLC analysis after stirring at room temperature for 30 min. Purification by chromatography using ethyl acetate-hexane (25:75) as eluent gave **42b** (159 mg, 68%) (as a 53:47 mixture of diastereomers) as a white, crystalline solid; mp 104−106 °C; $[\alpha]_{20}^{D}$ –35.8 (*c* 4 in ethanol); (Found C, 68.00; H, 6.71. $C_{21}H_{25}NO_3S$ requires C, 67.90; H, 6.78%); ν_{max}/cm^{-1} (KBr) 3337 (br NH), 1645 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.19, 1.26, 1.32, 1.39, 1.47 [2 × 3H, 2 × d, *J* 7, 7, C*H*$_3$C(4), C*H*$_3$C(5) and C(2)*H*$_3$], 3.55-3.86 [2H, m, C(4)*H* and C(5)*H*], 4.01, 4.02 (1H, d, *J* 2, C*H*S), 5.01-5.14 (1H, m, NC*H*), 5.46, 5.58 [1H, d, *J* 2, C(2)*H*], 7.12-7.42 (11H, m Ar*H* and N*H*); δ_C (67.8 MHz, $CDCl_3$) 16.0, 16.3, 16.9, 21.5, 21.6 [*C*H$_3$C(4), *C*H$_3$C(5), *C*(2)H$_3$], 48.95 (N*C*H), 57.4, 58.4 (*C*HS), 79.4, 79.6, 80.2, 80.4 [*C*(4)H and *C*(5)H], 101.5, 101.9 [*C*(2)H], 126.0, 126.4, 127.2, 127.5, 128.5, 128.9, 130.4, 130.7 (aromatic *C*H), 134.0, 142.8 (aromatic *C*), 166.9, 167.0 (*C*O); MS *m/z* 371 (M^+, 25%), 262 (14%), 101 [100%, $(C_5H_9O_2)^+$], 91 (53%), 78 (84%).

(4*S*,5*S*)-4,5-Dimethyl-2-[(S)-*N*-(1-phenylethyl)-2-(phenylthio)acetamide]-1,3-dioxolane 43b

This was prepared following the procedure described for **42a** using **1b** (0.20 mg, 0.63 mmol), **41b** (119 mg, 1.32 mmol), *n*-butyllithium (0.79 mL, 1.6 M in hexane, 1.26 mmol) and THF (3 and 3 mL). The reaction was complete (by TLC analysis) after stirring at room temperature for 30 min. Purification by chromatography using ethyl acetate-hexane (25:75) as eluent gave **43b** (174 mg, 75%) (as a 51:49 mixture of diastereomers) as a white, crystalline solid; mp 106-108 °C; [α] –19.4 (*c* 6 in ethanol); (Found C, 68.00; H, 7.00; N, 3.61; S, 8.85. $C_{21}H_{25}NO_3S$ requires C, 67.90; H, 6.78; N, 3.77; S, 8.63%); ν_{max}/cm^{-1} (KBr) 3259 (NH), 1647 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.25, 1.21, 1.34, 1.40, 1.47 [2 × 3H, 2 × d, *J* 7, 7, C*H*$_3$C(4), C*H*$_3$C(5) and C(2)*H*$_3$], 3.63-3.77 [2H, m, C(4)*H* and C(5)*H*], 4.00, 4.02 (1H, d, *J* 3, C*H*S), 5.02-5.15 (1H, m, NC*H*), 5.53 [1H, d, *J* 2, C(2)*H*], 7.04-7.43 (11H, m, Ar*H*, N*H*); δ_C (67.8 MHz, $CDCl_3$) 16.1, 16.3, 16.9, 17.0, 21.7, 21.8 [*C*H$_3$C(4), *C*H$_3$C(5) and *C*H$_3$CHPh], 48.85, 48.90 (N*C*H), 57.7, 58.3 (*C*HS), 79.3, 79.6, 80.26, 80.33 [*C*(4)H and *C*(5)H], 101.76,

101.80 [*C*(2)H], 126.0, 126.1, 127.0, 127.2, 128.5, 128.6, 129.1, 129.2, 130.5, 130.6 (aromatic *C*H), 133.9, 134.1, 142.9 (aromatic *C*, 3 signals for 4 carbons), 166.9, 167.1 (*C*O); MS *m/z* 371 (M^+, 33 %), 262 (14), 101 (100, $[C_5H_9O_2]^+$).

(4*R*, 5*R*)-4,5-Dimethyl-2-[*N*-benzyl-2-(phenylthio)-acetamide]-1,3-dioxolane 42c

This was prepared following the procedure described above for **42a** using **1c** (0.30 g, 1.00 mmol), **41a** (0.2 mL, 2.07 mmol) and *n*-butyllithium (91.2 mL, 1.97 mmol) in THF (12 mL), at room temperature over 2 h. Purification by chromatography on silica gel using ethyl acetate/hexane (20:80) as eluent gave **42c** as a white crystalline solid (0.23 g, 64%); mp 76-77 °C; $[\alpha]_{20}^{D}$ –15.0 (*c* 1.4 in CH_2Cl_2); (Found C, 67.10; H, 6.36; N, 4.10; S, 8.86; $C_{20}H_{23}NO_3S$ requires C, 67.20; H, 6.48; N, 3.92; S, 8.97%); ν_{max}/cm^{-1} (film) 3290 (NH), 2930 (CH), 1637 (C=O), 1560 (C=C); δ_H (270 MHz, $CDCl_3$) 1.20-1.35 (6H, m, 2 × C*H*$_3$), 3.64-3.85 [2H, m, 2 × OC*H*(CH_3)], 4.05-4.07 (1H, 2 × overlapping d appears as m, C*H*SPh), 4.37-4.56 (2H, m, NC*H*$_2$Ph), 5.54, 5.60 (1H, 2 × d, 47:53, *J* 2.4, 2.4, O_2C*H*), 7.12-7.43 (11H, m, Ar*H*, N*H*); δ_C (67.8 MHz, $CDCl_3$) 16.1, 16.2, 16.8, 16.9 (2 × *C*H$_3$), 43.7 (N*C*H$_2$Ph), 57.7, 58.5 (*C*HSPh), 79.3, 79.5, 80.2, 80.4 [2 × O*C*H(CH_3)], 101.7, 101.9 (O_2*C*H), 127.1, 127.3, 127.6, 128.7, 129.1, 130.4, 130.6 (aromatic *C*H, 7 signals seen), 134.0, 137.9 (aromatic *C*), 167.9 (*C*O); M.S. m/z 357 (M^+, 12%), 248 (5, $[M^+\text{-PhS}]^+$), 101 (100, $[C_5H_9O_2]^+$), 91 (74, $[CH_2Ph]^+$), 73 (68, $[SCHCO]^+$).

(4*S*,5*S*)-4,5-Dimethyl-2-[*N*-benzyl-2-(phenylthio)-acetamide]-1,3-dioxolane 43c

This was prepared following the procedure described above for **42a** using **1c** (0.30 g, 1.00 mmol), **41b** (0.2 mL, 2.07 mmol) and *n*-butyllithium (1.6 M solution in hexanes, 91.2 mL, 1.97 mmol) in THF (2 × 6mL). The reaction was complete after 2 h at room temperature. Purification by chromatography on silica gel using ethyl acetate/hexane (20:80) as eluent gave **43c** as a white crystalline solid (0.18g, 51%); mp 76-77 °C; $[\alpha]_{20}^{D}$ +15.7 (*c* 1 in CH_2Cl_2); ν_{max}/cm^{-1} (KBr) 3292 (NH), 2971 (CH), 1637 (C=O), 1560 (C=C); δ_H (270 MHz, $CDCl_3$) 1.18-1.35 (6H, m, 2 × C*H*$_3$), 3.62-3.84 [2H, m, 2 × OC*H*(CH_3)], 4.05-4.08 (1H, 2 × overlapping d appears as m, C*H*SPh), 4.36-4.56 (2H, m, NC*H*$_2$Ph), 5.54, 5.60 (1H, 2 × d, 48:52, *J* 2.4, 2.4, O_2C*H*), 7.12-7.44 (11H, m, Ar*H*, N*H*); δ_C (67.8 MHz, $CDCl_3$) 16.1, 16.3, 16.9, 17.0 (2 × C*H*$_3$), 43.7 (N*C*H$_2$Ph), 57.8, 58.6 (*C*HSPh), 79.3, 79.6, 80.3, 80.4 [2 × O*C*H(CH_3)], 101.8, 101.9 (O_2*C*H), 127.1, 127.4, 127.6, 128.3, 129.2, 130.4, 130.6 (aromatic *C*H, 7 signals seen), 134.2, 137.9 (aromatic *C*), 168.0 (*C*O).

(4*R*,6*R*)-4,6-Dimethyl-2-[*N*-benzyl-2-(phenylthio)-acetamide]-1,3-dioxolane 44c

This was prepared following the procedure described for **42a** using **1c** (0.08 g, 0.25 mmol), **41c** (0.06 g, 0.53 mmol) and *n*-butyllithium (1.6 M in hexanes, 0.3 mL, 0.51 mmol) in THF (4 mL), at room temperature for 2 h. Purification by chromatography on silica gel using ethyl acetate/hexane (25:75) as eluent gave the product **44c** as an oil (0.60 g, 61%) as an essentially equimolar mixture of diastereomers; (Found C, 68.00; H, 7.00; N, 3.97; S, 8.77; $C_{21}H_{23}NO_3S$ requires C, 67.89; H, 6.78; N, 3.77; S, 8.63%); ν_{max}/cm^{-1} (film) 3316 (NH), 2927 (CH), 1651 (CO), 1538 (C=C); δ_H (270 MHz, $CDCl_3$) 1.17-1.25 (3H, m, C*H*$_3$), 1.29-1.45 [4H, m, C*H*$_3$, C(5)H$_a$*H*$_b$], 1.75-1.90 [1H, m, C(5)*H*$_a$H$_b$], 3.95-4.11 [2H, m, C*H*SPh, OC(4)*H*(CH$_3$) or OC(6)*H*(CH$_3$)], 4.30-4.64 [3H, m, NC*H*$_2$Ph, OC(4)*H*(CH$_3$) or OC(6)*H*(CH$_3$)], 5.36-5.39 (1H, 2 × overlapping d appears as t, *J* 2.9, 3.4, O$_2$C*H*), 7.11-7.44 (11H, m, Ar*H*, N*H*); M.S. m/z 371 (M^+, 52%), 262 (63, $[M-PhS]^+$), 115 (100, $[C_6H_{11}O_2]^+$).

(4*R*,5*R*)-4,5-Diethoxycarbonyl-2-[N-benzyl-2-(phenylthio)acetamide]-1,3-dioxolane 45c

Diisopropylamine (0.2 mL, 1.35 mmol) was dissolved in THF (3 mL) at 0 °C, and *n*-butyllithium (1.6 M solution in hexanes, 0.8 mL, 1.32 mmol) was added. This was stirred for 15 min under nitrogen, and (-)-D-diethyl tartrate **41d** (0.2 mL, 1.39 mmol) was added. After stirring for a further 10 min, a solution of **1c** (0.20 g, 0.66 mmol) in THF (3 mL) was added. This reaction mixture was stirred under nitrogen for 19 h. The reaction was quenched with a saturated aqueous solution of ammonium chloride (10 mL), and ether (20 mL) was added. The layers were separated and the aqueous layer washed with ether (2 × 10 mL). The combined organic layers were washed with brine (15 mL), dried, and the solvent evaporated at reduced pressure to give the crude product mixture as an oil. ^{1}H NMR spectroscopic analysis showed that there was no trace of starting material **1c** remaining. However, there appeared to be a lot of diethyl tartrate remaining in the crude product mixture. A number of attempts were made to separate the product **45c** from the diethyl tartrate, including chromatography on silica gel using ethyl acetate/hexane (20:80) as eluent, and distillation, but were unsuccessful. The product contained a mixture of ~2:1 diethyl tartrate (DET) to product **45c** (as a mixture of two diastereomers in a ratio of 57:43), giving 4% recovery of the product; δ_H (270 MHz, $CDCl_3$) 1.23-1.42 (~18H, m, 6H due to C*H*$_3$CH$_2$O, 12H due to DET), 3.23 (~4H, br d, O*H* of DET), 4.02* (0.6H, d, *J* 4.6, C*H*S), 4.18-4.34 (4.4H, m, 2 × CH$_3$C*H*$_2$O, C*H*S), 4.43-4.49 (2H, m, NC*H*$_2$Ph), 4.54 (~4H, br d, DET), 4.73 [0.4H, d, *J* 4.0, C(4)*H*], 4.74-4.83* [1.2H, ABq, *J* 3.8, C(4)*H*, C(5)*H*], 4.93 [0.4H, d, *J* 4.3, C(5)*H*], 5.75*, 5.83 (1H, 2 × d, *J* 4.6, 4.6, O$_2$C*H*), 7.15-7.52 (11H, m, Ar*H*, N*H*).

*Major diastereomer.

(4*R*,5*R*)-4,5-Dimethyl-2-[*N*-(2-propenyl)-2-(phenylthio)acetamide]-1,3-dioxolane 42h

This was prepared following the procedure described for **42a** using **1h** (0.20 g, 0.79 mmol), **41a** (0.15 g, 1.66 mmol), *n*-butyllithium (0.98 mL, 1.6 M in hexane, 1.58 mmol) and THF (3 mL and 3 mL). The reaction was complete (by TLC analysis) after stirring at room temperature for 2 h. Purification by chromatography using ethyl acetate-hexane (25:75) as eluent gave **42h** (180 mg, 83%) (as a 52:48 mixture of diastereomers) as a white, crystalline solid; mp 58-60 °C; $[\alpha]_{20}^{D}$ –15.3 (*c* 6 in ethanol); (Found C, 62.14; H, 6.06; N, 4.51; S, 10.25. $C_{16}H_{21}NO_3S$ requires C, 62.51; H, 6.89; N, 4.56; S, 10.43%); ν_{max}/cm^{-1} (film) 3292 (NH), 1659 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.25, 1.27 [3 H, d, *J* 6, C*H*$_3$C(4) or C*H*$_3$C(5)], 1.32, 1.34 [3 H, d, *J* 6, C*H*$_3$C(4) or C*H*$_3$C(5)], 3.63-3.78 [2 H, m, C(4)*H* and C(5)*H*], 3.83-3.97 (2 H, m, NC*H*$_2$), 4.01, 4.02 (1 H, d, *J* 2, C*H*S), 5.05-5.18 (2 H, m, =C*H*$_2$), 5.54, 5.60 [1 H, d, *J* 2, C(2)*H*], 5.72-5.88 (1 H, m, C*H*=), 6.95, 7.05 (1 H, br s, N*H*), 7.22-7.43 (5 H, m, Ar*H*); δ_C (67.8 MHz, $CDCl_3$) 16.1, 16.3, 16.8, 16.9 [*C*H$_3$C(4) and *C*H$_3$C(5)], 41.9 (N*C*H$_2$), 57.9, 58.7 (*C*HS), 79.3, 79.6, 80.2, 80.4 [*C*(4)H and *C*(5)H], 101.7, 101.9 [*C*(2)H], 116.1, 116.2 (=*C*H$_2$), 127.0, 127.1, 129.1, 129.4, 130.3, 130.5, 133.7 (aromatic *C*H and *C*H=), 134.2, 134.3 (aromatic *C*), 167.8, 167.9 (*C*O); MS *m/z* 307 (M^+, 3 %), 262 (52), 101 (88, $[C_5H_9O_2]^+$).

(4*R*,6*R*)-4,6-Dimethyl-2-[*N*-(2-propenyl)-2-(phenylthio)acetamide]-1,3-dioxane 44h

This was prepared following the procedure described for the preparation of **42a** using **1h** (0.20 g, 0.79 mmol), **41c** (0.17 g, 1.66 mmol), *n*-butyllithium (0.99 mL, 1.6 M in hexane, 1.58 mmol) and THF (3 mL and 3 mL). The reaction was conducted at 0 °C and was complete (by TLC analysis) after stirring for 5 min. Purification by chromatography using ethyl acetate-hexane (25:75) as eluent gave **44h** (135 mg, 53%) (as a 51:49 mixture of diastereomers) as a white, crystalline solid; mp 47-49 °C; $[\alpha]_{20}^{D}$ –7.7 (*c* 11 in ethanol); (Found C, 63.82; H, 7.36; N, 4.40; S, 9.95. $C_{17}H_{23}NO_3S$ requires C, 63.52; H, 7.21; N, 4.36%); S, 9.98; ν_{max}/cm^{-1} (KBr) 3309 (NH), 1655 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.20, 1.24 [3H, d, *J* 6, C*H*$_3$C(4) or C*H*$_3$C(6)], 1.35, 1.39 [3H, d, *J* 7, C*H*$_3$C(4) or C*H*$_3$C(6) and C(5)*H*$_A$H$_B$], 1.82-1.93 [1H, ddd, *J* 25, 13, 6, C(5)H$_A$*H*$_B$], 3.73-3.91 (2H, m, NC*H*$_2$), 3.90, 3.91 (1H, d, *J* 3, C*H*S), 3.95-4.18 [1H, m, C(4)*H* or C(6)*H*], 4.31-4.49 [1H, m, C(4)*H* or C(6)*H*], 5.07 (1H, dd, *J* 11, 1, =C*H*$_A$H$_B$), 5.17 (1H, dd, *J* 19, 1, =CH$_A$*H*$_B$), 5.35, 5.36 [1H, d, *J* 3, C(2)*H*], 5.70-5.87 (1H, m, C*H*=), 6.94, 7.06 (1H, br s, N*H*), 7.17-7.43 (5H, m, Ar*H*); δ_C (67.8

MHz, $CDCl_3$) 16.9, 21.5, 21.6 [*C*H_3C(4) and *C*H_3C(6)], 36.4 [*C*(5)H_2], 41.69, 41.72 (N*C*H_2), 57.2, 57.3 (*C*HS), 68.07, 68.14, 68.7, 68.8 [*C*(4)H and *C*(6)H], 93.1, 93.3 [*C*(2)H], 115.5, 115.7 (*C*H_2=), 126.8, 128.9, 130.2 (aromatic *C*H), 133.8 (*C*H=), 134.4 (aromatic *C*), 168.2, 168.3 (*C*O); MS *m/z* 321 (M^+, 1 %), 115 (90, $[C_6H_{11}O_2]^+$), 69 (100).

(4*R*,5*R*)-4,5-Dimethyl-2-[2-(phenylthio)acetamide]-1,3-dioxolane 42k

This was prepared following the procedure described for **42a** using **1k** (0.20 g, 0.94 mmol), **41a** (167 mg, 1.86 mmol), *n*-butyllithium (1.18 mL, 1.6 M in hexane, 1.88 mmol) and THF (3 mL and 3 mL). The reaction was complete (by TLC analysis) after stirring at room temperature for 0.5 h. Purification by chromatography using ethyl acetate-hexane (50:50) as eluent gave **42k** (143 mg, 80%) (as a 53:47 mixture of diastereomers) as a grey solid which did not require further purification; mp 98-100 °C; $[\alpha]_{20}^{D}$ –16.1 (*c* 6 in ethanol); (Found C, 58.06; H, 6.00; N, 5.60; S, 11.54. $C_{13}H_{17}NO_3S$ requires C, 58.41; H, 6.41; N, 5.29; S, 11.99%); ν_{max}/cm^{-1} (KBr) 3386 (NH), 1654, 1578 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.25, 1.27 [3H, d, *J* 6, C*H*$_3$C(4) or C*H*$_3$C(5)], 1.34, 1.35 [3H, d, *J* 6, C*H*$_3$C(4) or C*H*$_3$C(5)], 3.55-3.87 [2H, m, C(4)*H* and C(5)*H*], 3.92, 3.93 (1H, d, *J* 2, C*H*S), 5.52, 5.56 [1H, d, *J* 3, C(2)*H*], 5.89 (1H, br s, N*H*), 6.71 (1H, br s, N*H*), 7.18-7.46 (5H, m, Ar*H*), additional signals at 1.17-1.23 (m), 4.05-4.08 (2d or dd), 5.43-5.48 (m), 8.75-8.83 (dd or 2d), 9.55-9.70 (br s) due possibly to a rotamer; δ_C (67.8 MHz, $CDCl_3$) 16.1, 16.4, 16.9, 17.0 [*C*H_3C(4) and *C*H_3C(5)], 57.6, 58.2 (*C*HS), 79.4, 79.7, 80.4, 80.5 [*C*(4)H and *C*(5)H], 101.6, 101.8 [*C*(2)H], 126.4, 126.6 (aromatic *C*), 127.3, 127.4, 129.2, 129.4, 130.7, 130.9 (aromatic *C*H), 170.9 (*C*O); MS *m/z* 267 (M^+, 1%), 238 (1), 109 (20, $[PhS]^+$), 101 (100, $[C_5H_9O_2]^+$).

(4*R*,6*R*)-4,6-Dimethyl-2-[2-(phenylthio)acetamide]-1,3-dioxane 44k

This was prepared following the procedure described for the preparation of **42a** using **1k** (0.20 g, 0.94 mmol), **41c** (0.21 g, 1.97 mmol), *n*-butyllithium (1.18 mL, 1.6 M in hexane, 1.88 mmol) and THF (3 mL and 3 mL). The reaction was conducted at 0 °C and was complete (by TLC analysis) after stirring for 5 min. Purification by chromatography using ethyl acetate-hexane (50:50) as eluent gave **44k** (166 mg, 63 %) (as a 1:1 mixture of diastereomers) as a white, crystalline solid; mp 103-105 °C; $[\alpha]_{20}^{D}$ +15.5 (*c* 6 in ethanol); (Found C, 59.52; H, 6.99; N, 4.99; S, 10.95. $C_{14}H_{19}NO_3S$ requires C, 59.76; H, 6.81; N, 4.98; S, 11.40%); ν_{max}/cm^{-1} (film) 3444 (NH), 1682, 1582 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.21, 1.24 [3H, d, *J* 6, C*H*$_3$C(4) or C*H*$_3$C(6)], 1.33, 1.38 [3H, d, *J* 7, C*H*$_3$C(4) or C*H*$_3$C(6)],

1.35-1.52 [1H, m, C(5)H_AH$_B$], 1.82-1.94 [1H, ddd, *J* 25, 13, 6, C(5)H$_A$$H_B$], 3.81, 3.82 (1H, d, *J* 4, C*H*S), 3.94-4.14 [1H, m, C(4)*H* or C(6)*H*], 4.32-4.50 [1H, m, C(4)*H* or C(6)*H*], 5.31, 5.32 [1H, d, *J* 4, C(2)*H*], 5.97 (1H, br s, N*H*), 6.74, 6.79 (1H, br s, N*H*), 7.18-7.50 (5H, m, Ar*H*) additional signals due possibly to a rotamer also seen; δ_C (67.8 MHz, $CDCl_3$) 17.2, 22.0 [*C*H$_3$C(4) and *C*H$_3$C(6)], 36.7 [*C*(5)H$_2$], 57.1, 57.3 (*C*HS), 68.5, 68.6, 69.2, 69.3 [*C*(4)H and *C*(6)H], 93.49, 93.5 [*C*(2)H], 126.5, 129.5, 131.0 (aromatic *C*H), 134.6, 134.7 (aromatic *C*), 171.6, 171.7 (*C*O); MS *m/z* 281 (M^+, 2 %), 123 (22), 115 (95, $[C_6H_{11}O_2]^+$).

(4*R*,5*R*)-4,5-Dimethyl-2-[*N*,*N*-diphenyl-2-(phenylthio)acetamide]-1,3-dioxolane 42n

This was prepared following the procedure described for **42a** using a mixture of *E* and *Z* isomers (*ca.* 1:1) of **1n** (0.20 g, 0.55 mmol), **41a** (104 mg, 1.16 mmol), *n*-butyllithium (0.69 mL, 1.6 M in hexane, 1.1 mmol) and THF (3 mL and 3 mL). After stirring for 16 h at room temperature the reaction was complete (by TLC analysis). Purification by chromatography using ethyl acetate-hexane (20:80) as eluent gave **42n** (0.17 g, 75%) (as a 56:44 mixture of diastereomers) as a white, crystalline solid which did not require further purification; mp 99-100 °C; $[\alpha]_{20}^{D}$ –16.3 (*c* 8 in ethanol); (Found C, 71.88; H, 6.18; N, 3.30; S, 7.25. $C_{25}H_{25}NO_3S$ requires C, 71.57; H, 6.01; N, 3.34; S, 7.64%); ν_{max}/cm^{-1} (KBr) 1669, 1596 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.14, 1.19 [3H, d, *J* 6, C*H*$_3$C(4) or C*H*$_3$C(5)], 1.25, 1.27 [3H, d, *J* 6, C*H*$_3$C(4) or C*H*$_3$C(5)], 3.43-3.50, 3.50-3.62, 3.64-3.83 [2H, 0.5:0.5:1, m, C(4)*H* and C(5)*H*], 3.85, 3.86 (1H, d, *J* 7, C*H*S), 5.54, 5.55 [1H, d, *J* 7, C(2)*H*], 6.99-7.44 (15H, m, Ar*H*); δ_C (67.8 MHz, $CDCl_3$) 16.5, 16.7, 16.87, 16.94 [*C*H$_3$C(4) and *C*H$_3$C(5)], 53.2, 53.7 (*C*HS), 78.4, 78.6, 80.0, 80.1 [*C*(4)H and *C*(5)H], 103.6, 103.8 [*C*(2)H], 126.11-129.65 (complex mixture of signals), 133.3, 133.8 (aromatic *C*H), 142.4 (broad quaternary aromatic *C*), 168.97, 169.02 (*C*O); MS *m/z* 419 (M^+, 1 %), 167 (17), 101 (100, $[C_5H_9O_2]^+$), 73 (68).

(4*R*,6*R*)-4,6-Dimethyl-2-[*N*,*N*-diphenyl-2-(phenylthio)acetamide]-1,3-dioxane 44n

This was prepared following the procedure described for the preparation of **42a** using a mixture of *E* and *Z* isomers (*ca.* 1:1) of **1n** (0.20 g, 0.55 mmol), **41c** (0.12 g, 1.16 mmol). *n*-butyllithium (0.69 mL, 1.6 M in hexane, 1.1 mmol) and THF (3 mL and 3 mL). The addition was conducted at 0 °C, then the reaction mixture was allowed to warm slowly to room temperature. The reaction was complete (by TLC analysis) after stirring at room temperature for 16 h. Purification by chromatography using ethyl acetate-hexane (15:85) as eluent gave **44n** (0.17 g, 71%) (as a 51:49 mixture of diastereomers) as a viscous oil; $[\alpha]_{20}^{D}$ +4.1 (*c* 7 in

ethanol); ν_{max}/cm^{-1} (KBr) 1668, 1593 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.17, 1.25 [3H, d, *J* 6, C*H*$_3$C(4) or C*H*$_3$C(6)], 1.36 [3H, d, *J* 7, C*H*$_3$C(4) or C*H*$_3$C(6)], 1.60 [1H, br s, C(5)H_AH$_B$], 1.75-1.88 [1H, ddd, *J* 25, 14, 6, C(5)H$_A$$H_B$], 3.95, 4.02 (1H, d, *J* 8, C*H*S), 3.94-4.09 , 4.27-4.38 [2H, m, C(4)*H* and C(6)*H*], 5.26, 5.29 [1H, d, *J* 8, C(2)*H*], 6.95-7.77 (15H, m, Ar*H*); δ_C (67.8 MHz, $CDCl_3$) 17.0, 21.6, 21.8 [*C*H$_3$C(4) and *C*H$_3$C(6)], 36.68, 36.73 [*C*(5)H$_2$], 52.7, 52.9 (*C*HS), 67.9, 68.6 [*C*(4)H and *C*(6)H], 94.9, 95.23 [*C*(2)H], 125.9, 126.1, 126.4, 127.5, 127.9, 128.7, 129.7 (aromatic *C*H), 132.9, 133.3 (aromatic *C*), 134.2, 134.5 (aromatic *C*H), 142.2, 142.7 (aromatic *C*), 168.9, 169.5 (*C*O); MS *m/z* 433 (M^+, 9 %), 238 (29), 115 (67, $[C_6H_{11}O_2]^+$), 91 (100); Found (HRMS, EI) M^+ 433.17400 $C_{26}H_{27}NO_3S$ requires *m/z* 433.17117.

(4*R*,5*R*)-4,5-Di(ethoxycarbonyl)-2-[*N*,*N*-diphenyl-2-(phenylthio)acetamide]-1,3-dioxolane 45n

This was prepared following the procedure described for the preparation of **42a** using a mixture of *E* and *Z* isomers (*ca.* 1:1) of **1n** (0.20 g, 0.55 mmol), **41d** (0.24 mg, 1.16 mmol), *n*-butyllithium (0.69 mL, 1.6 M in hexane, 1.1 mmol), DIPA (0.16 mL, 1.13 mmol) and THF (3 mL and 3 mL). The reaction was complete (by TLC analysis) after stirring at room temperature for 18 h. Purification by chromatography using ethyl acetate-hexane (30:70) as eluent gave **45n** (0.14 g, 47%) (as a 59:41 mixture of diastereomers) as a colourless oil; $[\alpha]_{20}^{D}$ –48.9 (*c* 8 in ethanol); ν_{max}/cm^{-1} (film) 1748 (CO ester), 1668, 1593 (CO amide); δ_H (270 MHz, $CDCl_3$) (The signals corresponding to the major isomer are indicated by ◊), 1.14 (1.5H, t, *J* 7, C*H*$_3$CH$_2$O of one diastereomer), 1.36-1.41 (4.5H, m, C*H*$_3$CH$_2$O), 4.02-4.33 (5H, m, OC*H*$_2$, C*H*S), 4.69-4.86 [2H, m, C(4)*H* and C(5)*H*], 5.78$^{◊}$, 5.84 [1H, d, *J* 8, C(2)*H*], 7.12-7.46 (15H, m, Ar*H*); δ_C (67.8 MHz, $CDCl_3$) 14.07, 14.13 (*C*H$_3$CH$_2$O), 51.2$^{◊}$, 52.6 (*C*HS), 61.8$^{◊}$, 62.1 (O*C*H$_2$), 77.8$^{◊}$, 78.2 [*C*(2)H], 107.4$^{◊}$, 108.1 [*C*(4)H and *C*(5)H], 126.18-129.44 (complex series of signals, aromatic *C*H), 131.9, 132.7 (aromatic *C*), 133.7, 134.0 (aromatic *C*H), 142.1 (aromatic *C*), 168.1, 168.3, 168.8, 169.0 (*C*O amide and ester); MS *m/z* 535 (M^+, 2 %), 388 (23, M^+-2CO$_2$Et -H), 262 (50), 220 (64), 169 (100, $[NHPh_2]^+$), 134 (59); Found (HRMS, EI) M^+ 535.16040 $C_{29}H_{29}NO_7S$ requires *m/z* 535.16648.

(4*R*,5*R*)-4,5-Dimethyl-2-[*N*-(4-methylphenyl)-2-(*n*-butylthio)acetamide]-1,3-dioxolane 42r

This was prepared following the procedure described for **42a** using **1r** (0.20 g, 0.71 mmol), **41a** (134 mg, 1.49 mmol), *n*-butyllithium (0.89 mL, 1.6 M in hexane, 1.42 mmol) and THF (3 mL and 3 mL). The reaction was complete (by TLC analysis) after stirring for 1.5 h at room temperature. Purification by chromatography using ethyl acetate-hexane (15:85) as eluent gave **42r** (61 mg, 26 %) (as an ~ 1:1 mixture of diastereomers) as an off-white, crystalline solid which does not require further purification; 91-93 °C; $[\alpha]_{20}^{D}$ –12.3 (*c* 6 in ethanol); ν_{max}/cm^{-1} (film) 3303 (NH), 1654, 1605 (CO amide); δ_H (270 MHz, $CDCl_3$) 0.89 [3H, t, *J* 7, C(4′)H_3], 1.23-1.26 [3H, d, *J* 6, CH_3C(4) or CH_3C(5)], 1.29, 1.31 [3H, d, *J* 6, CH_3C(4) or CH_3C(5)], 1.32-1.49 [2H, m, C(3′)H_2], 1.54-1.69 [2H, m, C(2′)H_2], 2.32 (3H, s, ArCH_3), 2.59-2.73 (2H, m, SCH_2), 3.65 (1H, d, *J* 2, C*H*S), 3.66-3.84 [2H, m, C(4)*H* and C(5)*H*], 5.47, 5.51 [1H, d, *J* 2, C(2)*H*], 7.12-7.46 (4H, ABq, *J* 8, Ar*H*), 8.58, 8.65 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 13.5 [*C*(4′)H_3], 16.3, 16.9 [*C*H_3C(4) and *C*H_3C(5)], 20.8 (Ar*C*H_3), 21.8 [*C*(3′)H_2], 31.4 [*C*(2′)H_2], 32.24 [*C*(3′)H_2], 55.4, 56.3 (*C*HS), 79.3, 79.4, 80.2, 80.3 [*C*(4)H and *C*(5)H], 101.85, 101.94 [*C*(2)H], 119.5, 119.7, 129.4 (aromatic *C*H), 133.8, 133.9, 135.2 (aromatic *C*), 166.8, 166.9 (*C*O); MS *m/z* 337 (M^+, 55 %), 249 (20), 204 (18), 101 (100, $[CH(OCHCH_3)_2]^+$); Found (HRMS, EI) M^+ 337.17120 $C_{18}H_{27}NO_3S$ requires *m/z* 337.17117.

(4*R*,6*R*)-4,6-Dimethyl-2-[*N*-(4-phenylmethyl)-2-(*n*-butylthio)acetamide]-1,3-dioxane 44r

This was prepared following the procedure described for the preparation of **42a** using **1r** (0.16 g, 0.56 mmol), **41c** (117 mg, 1.13 mmol), *n*-butyllithium (0.74 mL, 1.6 M in hexane, 1.18 mmol) and THF (3 mL and 3 mL) but at 0 °C. The reaction was complete (by TLC analysis) after stirring at room temperature for 1.5 h. Purification by chromatography using ethyl acetate-hexane (15:85) as eluent gave **44r** (50 mg, 25%) (as a 53:47 mixture of diastereomers) as a yellow oil; $[\alpha]_{20}^{D}$ –3.7 (*c* 3 in ethanol); ν_{max}/cm^{-1} (film) 3320 (NH), 1663, 1603 (CO amide); δ_H (270 MHz, $CDCl_3$) 0.86 [3H, t, *J* 7, C(4′)H_3], 1.17, 1.28 [3H, d, *J* 6, CH_3C(4) or CH_3C(6)], 1.36, 1.39 [3H, d, *J* 6, CH_3C(4) or CH_3C(6)], 1.32-1.46 [2H, m, C(3′)H_2], 1.55-1.68 [3H, m, C(2′)H_2, C(5)H_AH$_B$], 1.81-1.96 [1H, ddd, *J* 25, 13, 6, C(5)H$_A$$H_B$], 2.32 (3H, s, ArC$H_3$), 2.62-2.74 (2H, m, SC$H_2$), 3.50, 3.52 (1H, d, *J* 3, C*H*S), 3.97-4.13 [1H, m, C(4)*H* or C(6)*H*], 4.36, 4.44 [1H, m, C(4)*H* or C(6)*H*], 5.28, 5.30 [1H, d, *J* 3, C(2)*H*], 7.12-7.47 (4H, ABq, *J* 8, Ar*H*), 8.70, 8.74 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 13.6 [*C*(4′)H_3], 16.9, 20.9, 21.8, 21.9 [*C*H_3C(4), *C*H_3C(6), Ar*C*H_3, *C*(3′)H_2], 31.3 [*C*(2′)H_2], 32.1 (S*C*H_2), 36.5, 36.6 [*C*(5)H_2], 55.1, 55.4 (*C*HS), 68.2, 68.3, 68.7, 69.0 [*C*(4)H and *C*(6)H],

93.35, 93.44 [*C*(2)H], 119.6, 119.7, 129.5 (aromatic *C*H), 133.8, 135.6 (aromatic *C*), 167.6 (*C*O); MS *m/z* 351 (M^+, 29 %), 263 (32), 146 (32), 115 (100, $[C_6H_{11}O_2]^+$); Found (HRMS, EI) M^+ 351.18712 $C_{19}H_{29}NO_3S$ *m/z* 351.18682.

(4*R*,5*R*)-4,5-Dimethyl-2-methyl-2-[*N*-(4-methylphenyl)-2-(phenylthio)acetamide]-1,3-dioxolane 42g

This was prepared following the procedure described for **42a** using **1g** (0.25 g, 0.79 mmol) (*ca*. equimolar mixture), **41a** (0.15 g, 1.66 mmol), *n*-butyllithium (0.99 mL, 1.6 M in hexane, 1.58 mmol) and THF (3 mL and 3 mL). The reaction was complete (by TLC analysis) after stirring for 16 h at room temperature. Purification by chromatography using ethyl acetate-hexane (15:85) as eluent gave **42g** (132 mg, 45%) (as a 54:46 mixture of diastereomers) as a yellow oil; $[\alpha]_{20}^{D}$ +4.5 (*c* 7 in ethanol); ν_{max}/cm^{-1} (film) 3330 (NH), 1615, 1600 (CO amide); δ_H (270 MHz, $CDCl_3$) 1.26, 1.28 [3H, d, *J* 6, C*H*$_3$C(4) or C*H*$_3$C(5)], 1.32, 1.35 [3H, d, *J* 6, C*H*$_3$C(4) or C*H*$_3$C(5)], 1.58, 1.60 [3H, s, C(2)*H*$_3$], 2.30 (3H, s, ArC*H*$_3$), 3.73-4.01 [2H, m, C(4)*H* and C(5)*H*], 4.02 (1H, s, C*H*S), 7.09-7.47 (9H, m, Ar*H*), 8.33, 8.41 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 15.9, 17.4 [*C*H$_3$C(4) and *C*H$_3$C(5)], 20.9 (Ar*C*H$_3$), 25.5, 25.9 [*C*(2)H$_3$], 63.4, 64.3 (*C*HS), 78.7, 79.2, 80.4, 80.7 [*C*(4)H and *C*(5)H], 108.0 [*C*(2)], 119.7, 119.9, 127.3, 127.4, 129.0, 129.1, 129.45, 129.49, 131.0, 131.2 (aromatic *C*H), 133.9, 134.1, 135.4 (aromatic *C*), 167.1, 167.4 (*C*O); MS *m/z* 371 (M^+, 1%), 267 (3), 115 (100); Found (HRMS, EI) M^+ 371.15480. $C_{21}H_{25}NO_3S$ requires *m/z* 371.15552.

(4*R*,6*R*)-4,6-Dimethyl-2-methyl-2-[*N*-(4-phenylmethyl)-2-(phenylthio)acetamide]-1,3-dioxane 44g

This was prepared following the procedure described for **42a** using **1g** (0.25 g, 0.79 mmol), **41c** (0.17 g, 1.66 mmol), *n*-butyllithium (0.99 mL, 1.6 M in hexane, 1.58 mmol) and THF (3 and 3 mL). The reaction was complete (by TLC analysis) after stirring at room temperature for 17 h. Purification by chromatography using ethyl acetate-hexane (20:80) as eluent gave **44g** (101 mg, 33%) (as a 73:27 mixture of diastereomers) as a colourless oil; $[\alpha]_{20}^{D}$ +2.9 (*c* 10 in ethanol); (Found C, 68.14; H, 7.48; N, 3.86; S, 8.46. $C_{22}H_{27}NO_3S$ requires C, 68.54; H, 7.06; N, 3.63; S, 8.32%); ν_{max}/cm^{-1} (film) 3324 (NH), 1661, 1601 (CO amide); δ_H (270 MHz, $CDCl_3$) (The signals corresponding to the major isomer are indicated by ◊) 1.14, 1.23, 1.28 [6H, d, *J* 7, C*H*$_3$C(4) and C*H*$_3$C(6), 3 signals for 4], 1.62, 1.65$^{◊}$ [3H, s, C(2)*H*$_3$], 1.57-1.82 [2H, m, C(5)*H*$_2$], 2.30 (3H, s, ArC*H*$_3$), 3.95 (1H, s, C*H*S), 4.06-4.27, 4.45-4.57 [2H, m,

C(4)*H* and C(6)*H*], 7.06-7.50 (9H, m, Ar*H*), 8.43, 8.54 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 20.8, 21.5, 22.3, 23.35, 23.40, 23.8 [Ar*C*H_3, *C*H_3C(4), *C*H_3C(6) and *C*(2)H_3], 38.7$^{\Diamond}$, 45.6 [*C*(5)H_2], 63.5$^{\Diamond}$, 65.9, 65.1, 65.4$^{\Diamond}$ [*C*(4)H and *C*(6)H, *C*HS], 99.9, 100.7$^{\Diamond}$ [*C*(2)], 119.5, 119.6, 125.1, 125.8, 127.0, 128.5, 129.0, 130.8 (aromatic *C*H), 133.55, 133.64, 134.3, 134.5, 134.8, 135.5 (aromatic *C*), 167.5$^{\Diamond}$, 170.4 (*C*O); MS *m/z* 385 (M^+, 13%), 223 (57), 129 (100, $[CHCH_3(OCHCH_3)_2CH_2]^+$).

(4*R*,5*R*)-4,5-Dimethyl-2-[*N*-benzyl-2-(*n*-butylthio)-acetamide]-1,3-dioxolane 42s

This was prepared following the procedure described for **42a** using **1s** (0.15 g, 0.53 mmol), **41a** (0.1 mL, 1.11 mmol) and *n*-butyllithium (1.6 M in hexanes, 0.7 mL, 1.06 mmol) in THF (6 mL) at room temperature for 2 h. Purification by chromatography on silica gel using ethyl acetate/hexane (20:80) as eluent gave the product **42s** as an oil (0.06 g, 39%); $[\alpha]_{20}^{D}$ –11.1 (*c* 0.1 in CH_2Cl_2); (Found C, 63.81; H, 8.19; N, 3.91; S, 9.43; $C_{18}H_{27}NO_3S$ requires C, 64.06; H, 8.06; N, 4.15; S, 9.50%); ν_{max}/cm^{-1} (film) 3282 (NH), 2930 (CH), 1644 (CO), 1556 (C=C); δ_H (270 MHz, $CDCl_3$) 0.83-0.97 [3H, m, C(4′)H_3], 1.17-1.30 (6H, m, 2 × CH_3), 1.30-1.45 [2H, m, C(3′)H_2], 1.48-1.62 [2H, m, C(2′)H_2], 2.53-2.70 (2H, m, SCH_2), 3.58-3.74 [3H, m, SC*H*, 2 × OC*H*(CH_3)], 4.48 (2H, d, *J* 5.9, NCH_2Ph), 5.42, 5.47 (1H , 2 × d, 50:50, *J* 2.7, 2.7, O_2C*H*), 7.14 (1H, br s, N*H*), 7.18-7.40 (5H, m, Ar*H*); δ_C (67.8 MHz, $CDCl_3$) 13.5 [*C*(4′)H_3], 16.09, 16.13, 16.8, 16.9 (2 × *C*H_3), 21.8 [*C*(3′)H_2], 31.4, 32.2 [S*C*H_2 and *C*(2′)H_2], 43.5 (N*C*H_2Ph), 54.5, 55.4 (S*C*H), 79.1, 79.2, 80.1, 80.2 [2 × O*C*H(CH_3)], 101.9, 102.0 (O_2*C*H), 127.3, 127.5, 127.6, 128.5 (aromatic *C*H), 138.2 (aromatic *C*), 168.7 (*C*O); M.S. m/z 337 (M^+,11%), 248 (80, [M-BuS]$^+$), 101 (100, $[C_5H_9O_2]^+$), 73 (89, $[SCHCO]^+$).

(4*S*,5*S*)-4,5-Dimethyl-2-[*N*-benzyl-2-(*n*-butylthio)-acetamide]-1,3-dioxolane 43s

This was prepared following the above procedure for **42a** using **1s** (0.15 g, 0.53 mmol), **41b** (0.1 mL, 1.11 mmol) and *n*-butyllithium (1.6 M in hexanes, 0.7 mL, 1.06 mmol) in THF (6 mL) at room temperature over 2 h. Purification by chromatography on silica gel using ethyl acetate/hexane (20:80) as eluent gave **43s** as an oil (0.04 g, 20%); $[\alpha]_{20}^{D}$ +11.9 (*c* 0.1 in CH_2Cl_2); ν_{max}/cm^{-1} (film) 3288 (NH), 2928 (CH), 1644 (CO); δ_H (270 MHz, $CDCl_3$) 0.85-0.92 [3H, m, C(4′)H_3], 1.19-1.28 (6H, m, 2 × CH_3), 1.30-1.44 [2H, m, C(3′)H_2], 1.49-1.62 [2H, m, C(2′)H_2], 2.56-2.68 (2H, m, SCH_2), 3.59-3.73 [3H, m, SC*H*, 2 × OC*H*(CH_3)], 4.49 (2H, d, *J* 6.2, NCH_2Ph), 5.43, 5.47 (1H, 2 × d, 50:50, *J* 2.7, 2.7, O_2C*H*), 7.15 (1H, br s, N*H*), 7.20-7.38 (5H, m, Ar*H*); δ_C

(67.8 MHz, $CDCl_3$) 13.5 [CH_3, *C*(4′)H_3], 16.16, 16.20, 16.86, 16.91 [CH_3, 2 × OCH(*C*H_3)], 21.9 [CH_2, *C*(3′)H_2], 31.5, 32.3 [CH_2, S*C*H_2 and *C*(2′)H_2], 43.7 (CH_2, N*C*H_2Ph), 54.7, 55.6 (CH, S*C*H), 79.2, 79.3, 80.2, 80.3 [CH, 2 × O*C*H(CH_3)], 102.0, 102.1 (CH, O_2*C*H), 127.4, 127.6, 128.6 (CH, aromatic *C*H), 138.3 (C, aromatic *C*), 168.8 (C, *C*O); M.S. m/z 337 (M^+, 8%), 248 (10, [M-BuS]$^+$), 101 (100, $[C_5H_9O_2]^+$), 73 (90, $[SCHCO]^+$), 43 (75, $[CONH]^+$).

Intramolecular nucleophilic addition

Treatment of 1u-*Z* with LiHMDS

This was conducted following the procedure described for **46a** using **1u**-*Z* (105 mg, 0.39 mmol), *n*-butyllithium (0.27 mL, 0.43 mmol), HMDS (94 μl, 0.45 mmol), THF (4 and 4 mL) with a reaction time of 16 h to give a mixture of products. Purification by chromatography using ethyl acetate-hexane (25:75) as eluent gave pure carboxanilide **46b** (Rf 0.3, ethyl acetate-hexane (25:75) as eluent) (10 mg, 11%) as a white crystalline solid; mp 94-95 °C; ν_{max}/cm^{-1} (film) 3300 (br NH), 1726, 1652 (CO α,β-unsaturated amide); δ_H (270 MHz, $CDCl_3$) 2.27 [3H, s, C(4)H_3], 2.99 (2H, overlapping dd, *J* 5, 4, CH_2S), 4.41 (2H, overlapping dd, *J* 5, 4, CH_2O), 7.10 (1H, t, *J* 7, Ar*H*), 7.33 (2H, dd, *J* 7, 8, Ar*H*), 7.52 (2H, d, *J* 8, Ar*H*), 7.91 (1H, br s, N*H*); δ_C (67.8 MHz, $CDCl_3$) 21.3 [*C*(4)H_3], 24.6 (*C*H_2S), 66.6 (*C*H_2O), 96.9 (S*C*=), 120.0, 124.2, 129.0 (aromatic *C*H), 138.1 (aromatic *C*), 156.7 (O*C*=), 164.2 (*C*O); MS *m/z* 235 (M^+, 50 %), 143 (100, M^+-NHPh), 103 (41), 93 (50); Found (HRMS, EI) *m/z* 235.06660 $C_{12}H_{13}NO_2S$ requires M^+ 235.06670.

Treatment of 1u-*E* with LiHMDS

The procedure used was as described for the reaction **1u**-*Z* with LiHMDS using **1u**-*E* (0.44 g, 1.62 mmol), *n*-butyllithium (1.11 mL, 1.78 mmol), HMDS (0.39 mL, 1.86 mmol) and THF (8 and 8 mL) to give a mixture of products. Purification by chromatography using ethyl acetate-CH_2Cl_2-hexane (25:5:75) as eluent gave carboxin **46b** (Rf 0.3 using ethyl acetate-hexane (25:75) as eluent) (27 mg, 7 %) as a white crystalline solid; ν_{max}/cm^{-1} (KBr) 3363 (NH), 1686, 1597 (CO α,β-unsaturated enamine ester); δ_H (270 MHz, $CDCl_3$) 2.50 (3H, s, CH_3C=), 3.12-3.19 (1H, m, C$H_A$$H_B$S), 3.34-3.40 (1H, m, C$H_A$$H_B$S), 4.25-4.33 (1H, m, C$H_A$$H_B$O), 4.80-4.88 (1H, m, C$H_A$$H_B$O), 7.16 (1H, t, *J* 8, Ar*H*), 7.58 (2H, overlapping dd, *J* 8, Ar*H*), 7.58 (2H, d, *J* 8, Ar*H*), 8.52 (1H, br s, N*H*).

Sulfur Nucleophiles

_N_-(4-Benzyl)-_Z_-3-phenylthio-2(benzylthio)propenamide 47v and _N_-(4-Benzyl)-3,3-di(phenylthio)-2(benzylthio)propanamide 48v

n-Butyllithium (0.65 mL, 1.6 M in hexane, 1.05 mmol) was added to a stirring solution of thiophenol (117 μL, 1.14 mmol) in THF (4 mL) at 0˚C. After stirring for 10 min at 0˚C and for 20 min at room temperature a solution of **1v** (0.30 g, 0.95 mmol) in THF (4 mL) was added dropwise. After 2 hours a further equivalent of lithium thiophenolate [from *n*-butyllithium (0.65 mL, 1.6 M in hexane, 1.05 mmol), thiophenol (117 μL, 1.14 mmol)] was added. TLC analysis showed the reaction had reached completion after 6 h and saturated aqueous ammonium chloride (10 mL) and ether (20 mL) were added. The phases were separated, the aqueous layer was extracted with ether (2 × 10 mL). The combined organic layers were washed with brine (3 × 10 mL), dried and evaporated to give the crude product (0.65 g) a pale yellow oil, ratio of **47v**:**48v** 1:3.3. Purification by column chromatography on silica gel using hexane:ethyl acetate (60-40% gradient elution ethyl acetate) gave **47v** (0.33g, 54%) as a yellow oil, and **48v** (0.20g, 41%) as a white solid.

47v: ν_{max}/cm^{-1} (film) 3282 (NH), 1644 (CO amide); δ_H (400 MHz, $CDCl_3$) 3.88 (2H, s, SC*H*$_2$Bn), 4.28 (2H, d, *J* 5.9, NHC*H*$_2$), 7.08-7.54 (15H, m, Ar*H*), 8.43 [1H, s, C(3)*H*]; δ_C (75.5 MHz, $CDCl_3$) 38.2 (CH_2, S*C*H$_2$), 44.1 (CH_2, *C*H$_2$NH), 119.8 (C, *C*S), 127.4, 127.5, 127.7, 128.5, 128.7, 129.0, 129.5 (7 × CH, aromatic *C*H), 131.2, 137.5, 138.1 (3 × C, aromatic *C*), 153.8 (CH, *C*HSPh), 163.4 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{23}H_{22}S_2NO$ ($M+H^+$) 392.1143. Found 392.1161 ($M+H^+$); m/z (ESI^+) 392.1 ($M+H^+$).

48v: ν_{max}/cm^{-1} (KBr) 3306 (NH), 1656 (CO amide); δ_H (400 MHz, $CDCl_3$) 3.57 (1H, d, *J* 3.8, C*H*S), 3.76 (1H, A of AB system, J_{AB} 12.0, one of SC*H*$_2$Bn), 3.79 (1H, B of AB system, J_{AB} 12.0, one of SC*H*$_2$Bn), 4.24 (2H, d, *J* 5.81, NC*H*$_2$Bn), 5.17 [1H, d, *J* 3.8, C(3)*H*], 6.97-7.43 (21H, m, N*H* and Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 38.0 (CH_2, S*C*H$_2$), 44.1 (CH_2, *C*H$_2$NH), 55.0 [CH, *C*H(SPh)$_2$], 61.6 (CH, *C*HS), 127.5, 127.7, 128.1, 128.7, 128.8, 129.0, 129.2, 131.7, 132.9 (9 × CH, aromatic *C*H), 133.6, 134.7, 136.9, 137.6 (4 × C, aromatic *C*), 168.3 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{29}H_{28}S_3NO$ ($M+H^+$) 502.1333. Found 502.1311 ($M+H^+$); m/z (ESI^-) 500.2 ($M-H^+$).

_N_-(4-Methylphenyl)-_Z_-3-phenylthio-2-(phenylsulfinyl)propenamide 49a-_Z_ and _N_-(4-Methylphenyl)-_E_-3-phenylthio-2-(phenylsulfinyl)propenamide 49a-_E_

Thiophenol (148 μL, 1.46 mmol) was added to a solution of **18a** (0.42 g, 1.32 mmol) in toluene (8 mL). The reaction mixture was stirred initially at room temperature for 2 h. Subsequent heating under reflux with stirring was necessary for the reaction to reach

completion after 7 h (TLC analysis). Dichloromethane (10 mL) was then added and the phases were separated. The aqueous layer was extracted with dichloromethane (2 × 10 mL), the combined organic layers were washed with sodium hydroxide (1M, 2 × 15 mL), distilled water (1 × 30 mL) and brine (1 × 30 mL), dried and evaporated to give the crude product (0.47g) as a yellow oil. The ^{1}H NMR spectrum of the crude material showed that the desired product had formed as a 1.1:1 diastereomeric mixture, in addition to *approx.* 12% **47a**. Purification by column chromatography on silica gel using hexane:ethyl acetate (60:40) as eluent gave **49a-*Z*** and **49a-*E*** as an off-white solid (327 mg, 63%) in a 1.6 : 1 diastereomeric mixture and **47a** as a white solid (60 mg, 12%).

49a-*Z*: ν_{max}/cm^{-1} (KBr) 3247 (br NH), 1668 (CO amide), 1024 (SO); δ_H (400 MHz, $CDCl_3$) 2.29 (3H, s, ArC*H*$_3$), 7.08-7.10 (2H, m, Ar*H*), 7.37-7.54 (10H, m, Ar*H*), 7.71-7.73 (2H, m, Ar*H*), 8.35 [1H, s, C(3)*H*], 10.20 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 20.9 (CH_3, Ar*C*H$_3$), 120.5, 124.0, 129.5, 129.7, 129.8, 131.2, 131.3, 131.4, 131.5 (9 × CH, aromatic *C*H), 132.5, 134.1, 135.2, 141.5 [4 × C, aromatic *C* and *C*(2)S], 151.6 [CH, *C*(3)H], 159.2 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{22}H_{20}NO_2S_2$ ($M+H^+$) 394.0935. Found 394.0942 ($M+H^+$); m/z (ESI^+) 394.0 ($M+H^+$).

49a-*E*: ν_{max}/cm^{-1} (KBr) 3433 (NH), 1663 (CO amide), 1020 (SO); δ_H (400 MHz, $CDCl_3$) 2.29 (3H, s, ArC*H*$_3$), 7.05-7.07 (2H, m, Ar*H*), 7.38-7.50 (8H, m, Ar*H*), 7.56-7.61 (4H, m, Ar*H*), 8.01 [1H, s, C(3)*H*], 9.83 (1H, br s, NH); δ_C (75.5 MHz, $CDCl_3$) 20.9 (CH_3, Ar*C*H$_3$), 120.3, 124.3, 126.9, 129.3, 129.5, 129.7, 129.8, 131.1, 131.3, 131.4 (10 × CH, aromatic *C*H), 127.0, 134.4, 134.8, 135.5, 141.8 [5 × C, aromatic *C* and *C*(2)S], 154.0 [CH, *C*(3)H], 160.6 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{22}H_{20}NO_2S_2$ ($M+H^+$) 394.0935. Found 394.0933 ($M+H^+$); m/z (ESI^+) 394.1 ($M+H^+$).