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Investigation of the chemoselective and enantioselective oxidation of α-thio-β-chloroacrylamides

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ABSTRACT

An investigation of the chemoselective and enantioselective oxidation of α-thio-β-chloroacrylamides is described. The α-thio-β-chloroacrylamides can be selectively oxidised to either the racemic sulfoxide or the sulfone very efficiently. The asymmetric sulfur oxidation of α-thio-β-chloroacrylamides is also discussed, with sulfoxide enantioselectivities of up to 52% ee achieved using the Kagan oxidation, and up to 71% ee when the Bolm oxidation is employed. While the enantioselectivities achieved are modest, these are among the most highly functionalised sulfides investigated in catalytic asymmetric oxidation, and the resulting enantioenriched sulfoxides have significant synthetic potential.

1. Introduction

Sulfoxides and sulfones are widely used in organic synthesis, particularly in carbon–carbon bond forming reactions.[1] These compounds are almost invariably prepared by oxidation of the corresponding thioethers. A variety of oxidants have been employed for this transformation.[2] Among the more common oxidants are *m*-CBPA,[3] CHP,[4] $NaIO_4$,[5] MMPP,[6] Oxone®,[7] H_2O_2[2] and MnO_4^-.[8]

The asymmetric synthesis of sulfoxides has received particular attention in recent years as the sulfoxide moiety has been shown to provide excellent stereochemical control as a chiral auxiliary. Furthermore, many enantiopure sulfoxides are known to have high biological activity.[9] Several methods are currently available for the preparation of optically active sulfoxides. The most generally used method is the Andersen method, which involves the nucleophilic addition of alkyl or aryl ligands to diastereochemically pure chiral sulfinates.[10] Despite the high yields of enantiopure sulfoxides obtained using this method, its scope is limited due to the difficult preparation and limited availability of suitable chiral precursors. The development of chiral precursors that possess two leaving groups[11,12] and the use of carbanionic leaving groups[13] have extended the scope of this methodology.

An attractive alternative to nucleophilic displacement is asymmetric sulfur oxidation. Very efficient biological sulfide oxidations have been reported using both whole cell systems and isolated enzymes.[14,15] Metal-free asymmetric sulfur oxidation has been reported using oxaziridines[16] and hydroperoxides.[17] The most popular route to asymmetric sulfur oxidation is metal-catalysed oxidation. The titanium-based Kagan oxidation method was first reported in the 1980s and is one of the most widely used oxidation methods; the amount of water present in these reactions must be carefully controlled.[18] The use of titanium/BINOL complex was later reported by Uemura et al.[19,20] A robust oxidation method based on vanadium was reported by Bolm and Bienewald.[21] This method involves the in situ formation of a catalyst from vanadyl acetylacetonate and a Schiff base. The oxygen source is hydrogen peroxide and critically the reaction is not moisture sensitive. Due to its ease of use, this method has recently attracted much attention, including an investigation of the nature of the species involved.[22,23]

Following our recent report[24] of the highly efficient and stereoselective transformation of α-thioamides to the corresponding α-thio-β-chloroacrylamide derivatives on treatment with NCS, we herein report the chemoselective and stereoselective oxidation of the β-chloroacrylamides to the sulfoxide and sulfone levels to extend the scope of this methodology. While the enantioselectivities achieved in the oxidation to the sulfoxide derivatives are modest (up to 71% ee), these are among the most highly functionalised sulfides investigated in catalytic asymmetric oxidation, and the resulting enantioenriched sulfoxides have significant synthetic potential, for example, as Michael acceptors, dienophiles or dipolarophiles.[25] Asymmetric oxidation of aryl methyl sulfides is readily achieved with high enantioselectivity using the Kagan and Bolm methods, among others; however, successful extension to differently substituted sulfides, or sulfides bearing additional functionality, has been remarkably limited.

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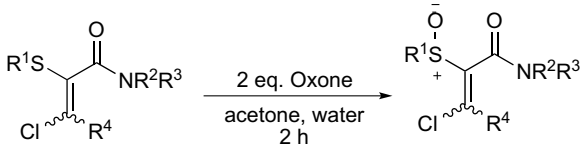
2. Results and discussion

2.1. Oxidation of the β-chloroacrylamides to the racemic sulfoxide

The chemoselective oxidation of **1a** to the racemic sulfoxide was investigated using a range of oxidising reagents. The use of H_2O_2, $KMnO_4$, peracetic acid and MMPP led to the recovery of the starting material **1a**, while *m*-CPBA gave a 1:1 mixture of sulfide and sulfoxide. Employing 2 equiv of Oxone® as oxidant in an acetone/water mixture led to complete conversion to the sulfoxide **2a**, and this reaction has been extended to a series of derivatives as summarised in Table 1. While most of the compounds explored had *Z*-stereochemistry, oxidation of a number of *E*-isomers was also undertaken equally efficiently and selectively. Critically, there was no evidence of sulfone formation in any instance.

Table 1
Oxidation to the racemic sulfoxide



R^1	R^2	R^3	R^4	*E*/*Z*	Product	% Yield[a]
Ph	Tol	H	H	*Z*	**2a**	96
Ph	Bn	H	H	*Z*	**2b**	98
Ph	*i*-Pr	H	H	*Z*	**2c**	98
Ph	Et	H	H	*Z*	**2d**	57
Ph	*n*-Bu	H	H	*Z*	**2e**	98
Ph	Allyl	H	H	*Z*	**2f**	98
Ph	H	H	H	*Z*	**2g**	92
Ph	4-F–C_6H_4	H	H	*Z*	**2h**	95
Ph	Me	Me	H	*E*	**2i**	98
n-Bu	4-F–C_6H_4	H	H	*Z*	**2j**	95
n-Bu	*n*-Bu	H	H	*Z*	**2k**	80
n-Bu	Bn	H	H	*Z*	**2l**	80
n-Bu	Tol	H	H	*Z*	**2m**	91
n-Bu	Ph	H	H	*Z*	**2n**	76
4′-$MeOC_6H_4$	Tol	H	H	*Z*	**2o**	84
4′-$MeOC_6H_4$	Bn	H	H	*Z*	**2p**	93
4′-$MeOC_6H_4$	Et	H	H	*Z*	**2q**	96
4′-$NO_2C_6H_4$	Tol	H	H	*Z*	**2r**	84
i-Bu	4-F–C_6H_4	H	H	*Z*	**2s**	92
i-Pr	4-F–C_6H_4	H	H	*Z*	**2t**	88
Me	4-F–C_6H_4	H	H	*Z*	**2u**	92
Me	*n*-Bu	H	H	*Z*	**2v**	85
Me	Bn	H	H	*Z*	**2w**	82
Bn	Bn	H	H	*Z*	**2x**	69
Bn	4-F–C_6H_4	H	H	*Z*	**2y**	77
Bn	*n*-Bu	H	H	*Z*	**2z**	69
Bn	Tol	H	H	*Z*	**2aa**	72
Bn	Me	H	H	*Z*	**2ab**	66
Bn	Ph	H	H	*Z*	**2ac**	76
Bn	H	H	H	*Z*	**2ad**	46
Bn	Me	Me	H	*E*	**2ae**	75
Bn	Me	Me	H	*Z*	**2af**	75
Bn	4-F–C_6H_4	H	Me	*Z*	**2ah**	83
Bn	4-F–C_6H_4	H	Me	*E*	**2ag**	53

[a] Yields quoted are following purification by column chromatography or recrystallisation.

Each of the sulfoxides was isolated as a crystalline solid and purified by column chromatography or recrystallisation. The relative stereochemistry (*E*/*Z*) of the β-chloroacrylamides was retained on oxidation to the sulfoxides in all cases, as confirmed by single crystal X-ray crystallography of the *N*-ethyl derivative **2d** (Fig. 1).

Analysis of the dihedral angles and rotation of the crystal structure illustrate that the sulfoxide moiety is twisted out of the plane of the acrylamide, presumably due to steric interactions between

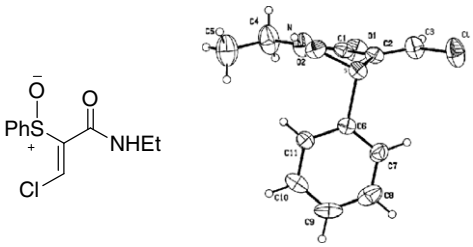


Figure 1. A view of **2d** showing the structure and stereochemistry. Anisotropic displacement parameters are drawn at the 30% probability level.

the phenyl ring of the sulfoxide and the chlorine atom. In all cases, an upfield shift in the ^1H NMR spectrum of the β-hydrogen of approximately 0.15 ppm occurred on oxidation of the β-chloroacrylamides, reflecting a significant impact on the extent of resonance delocalisation in the acrylamide system.

2.2. Oxidation to the sulfone

An investigation of the oxidation of sulfoxide **2a** to sulfone **3a** was undertaken with a range of oxidants, including H_2O_2, $KMnO_4$, peracetic acid, MMPP, Oxone® and *m*-CPBA, with *m*-CPBA the only oxidant resulting in oxidation to the sulfone. While the crude products were relatively clean by NMR, with sulfoxide oxidation complete, isolation of analytically pure sulfones from the oxidations is challenging, principally as the labile sulfones, potent Michael acceptors, are not stable on silica gel. To overcome this issue, morpholine was added to the crude sulfones, triggering a substitution process to the β-amino derivatives, as illustrated in Table 2. Critically, the morpholine adducts, which are stabilised by extensive delocalisation, are readily purified and characterised.

Following this protocol, a series of sulfoxides were treated with 2 equiv of *m*-CPBA in DCM. Following stirring at room temperature for 24 h, 4 equiv of morpholine was added. TLC analysis indicated reaction completion after 15 min and following purification by column chromatography, the morpholine adduct of the sulfone **4** was isolated (see Table 2).

In conclusion, the chemoselective oxidation of the β-chloroacrylamides to either the sulfoxide or sulfone level is readily achieved. For ease of characterisation, the sulfones were trapped as adducts with morpholine.

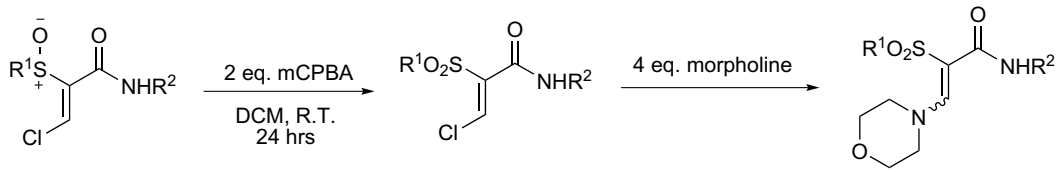
2.3. Asymmetric sulfur oxidation of the β-chloroacrylamides

A number of methods for the enantioselective oxidation of the β-chloroacrylamides were examined, including Kagan oxidation[18] and Bolm oxidation.[21]

2.3.1. Kagan oxidation

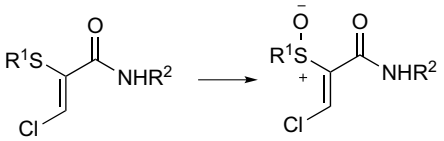
When the β-chloroacrylamide **1a** was oxidised under standard Kagan conditions employing a ratio of $Ti(O^iPr)_4$/(+)-DET/H_2O/β-chloroacrylamide of 1:2:1:2, using cumene hydroperoxide (2 equiv, i.e., equimolar with the sulfide) as oxidant, the conversion of the β-chloroacrylamide **1a** to the sulfoxide **2a** was determined to be 46% by ^1H NMR spectroscopy of the crude reaction product. Following removal of the 2-phenylpropan-2-ol by-product by distillation, the sulfoxide **2a** was isolated in 30% yield after chromatography on silica gel. However, the enantiomeric ratio of the product was then determined to be just 12% ee by chiral HPLC. The standard Kagan oxidation of methyl tolyl sulfide using the same reagents was undertaken to ensure that the oxidising agent was correctly formed. Methyl tolyl sulfoxide was isolated in 84% ee, a value which compares quite favourably with the reported value of 89% ee.[26]

Table 2
Oxidation to the sulfone



R^1	R^2	Sulfone	% Yield
Ph	Tol	**4a**	42
Ph	Me	**4b**	30
Bn	Bn	**4c**	42
Bn	4-F–C_6H_4	**4d**	43
Bn	*n*-Bu	**4e**	63
Bn	Tol	**4f**	56
Bn	Me	**4g**	38
Bn	Ph	**4h**	56
Bn	H	**4i**	37
n-Bu	Bn	**4j**	38
n-Bu	Tol	**4k**	45
n-Bu	Ph	**4l**	54

Table 3
Asymmetric oxidation using the Kagan oxidation



1	R^1	R^2	Method	Sulfoxide	% Conversion[a]	% Yield[b]	% ee[c]	[α][d]
2	Ph	Tol	A	**2a**	46	30	12	–
3	Ph	Et	A	**2d**	0	–	–	–
4	*n*-Bu	Bn	A	**2l**	0	–	–	–
5	4-NO_2–C_6H_4	Tol	A	**2r**	20	9	4	–
6	4-MeO–C_6H_4	Tol	A	**2o**	40	28	30[e]	–
7	*n*-Bu	Tol	A	**2m**	60	49	51	−84
8	Ph	4-F–C_6H_4	A	**2h**	60	40	25	–
9	*n*-Bu	4-F–C_6H_4	A	**2j**	100	68	51	−98
10	*n*-Bu	4-F–C_6H_4	A	**2j**	100	68	52	+94
11	Me	Tol	A	**2ai**	100	66	39	−72
12	Me	4-F–C_6H_4	A	**2u**	72	65	43	–
13	*i*-Bu	4-F–C_6H_4	A	**2s**	75	68	17	
14	*i*-Bu	Tol	A	**2aj**	73	65	7	
15	Ph	Tol	B	**2a**	13	9	15	–

Method A: standard Kagan oxidation using (+)-DET except entry 10, which used (−)-DET.
Method B: modified Kagan oxidation using 0.1 equiv of the catalyst.
[a] As determined by ^{1}H NMR spectroscopy of the crude product mixture
[b] Yield after chromatography on silica gel.
[c] Enantiomeric ratios were determined by chiral HPLC using IPA/hexane as mobile phase on a Chiralcel AS column detected at λ 254 nm.
[d] All specific rotations were recorded as solutions in DCM (*c* 1.3–2.0).
[e] As determined by chiral shift NMR spectroscopy using (+)-Eu(hfc)$_3$ as chiral shift reagent.

Extension of the initial work with sulfoxide **2a** to the enantioselective oxidation of a series of β-chloroacrylamides using the Kagan reagent was next undertaken as summarised in Table 3. In all cases, with the exception of entry 10, (+)-DET was used and the (*S*)-sulfoxide series was formed.

Significantly, oxidation was only observed for *N*-aryl derivatives, with partial or complete oxidation to the sulfoxides seen under the standard Kagan oxidation conditions, albeit with modest enantioselectivity.

Investigation of the impact of substitution on the phenylthio group was first explored. Introduction of *p*-nitro or methoxy groups resulted in a decrease in the efficiency of oxidation, but the enantioselectivity altered significantly, reflecting the variation in the electronic properties of the sulfide. In the presence of the 4-MeO–C_6H_4 group (Table 3, entry 6), an increase in selectivity to 30% ee resulted, while in the presence of 4-NO_2–C_6H_4 group (Table 3, entry 5) a decrease to 4% ee resulted, cf. 12% ee in the unsubstituted derivative (Table 3, entry 1).

Investigation of the alkylthio derivatives proved interesting. Replacement of the phenylthio moiety with the more electron donating *n*-butylthio group resulted in improved conversion and enantioselectivity (Table 3, entry 7), with 51% ee while using the *N*-tolyl group.

The effect of the nature of the amide group was next examined. It had already been shown that on replacement of *N*-tolyl amide with the relatively less electron withdrawing *N*-benzyl or *N*-ethyl

group, no oxidation occurred. Thus we decided to look at incorporating a more electron withdrawing amide by synthesising the *N*-4-fluoroaniline phenylthio and *n*-butylthio derivatives.

When the β-chloroacrylamides **1h** and **1j** were exposed to the standard Kagan oxidation conditions, an improvement in both reaction efficiency and selectivity was recorded for both compounds compared to **1a**. For **1h** (Table 3, entry 8), the increase in the degree of conversion was moderate, up from 46% for **1a** to 60% for **1h**, as was the increase in the enantioselectivity, up from 12% ee for **1a** to 25% ee for **1h**. Some of the sulfoxide (+)-**2h** isolated from the oxidation of **1h** was recrystallised from ether/hexane and the mother liquor was found to contain (+)-**2h** in 32% ee. Subsequent analysis of the solid isolated from the recrystallisation showed that the sulfoxide precipitates as a racemate.

The use of **1j** (Table 3, entry 9) gave much better results than those obtained with any other β-chloroacrylamide. Complete conversion of the β-chloroacrylamide **1j** to the corresponding sulfoxide **2j** occurred, with **2j** isolated in 68% yield after removal of the 2-phenyl-2-propanol and chromatography of the residue on silica gel. Analysis of the enantiomeric ratio of the material by chiral HPLC showed almost identical selectivity to that seen with **2m**, with the sulfoxide **2j** having 51% ee. The result of this reaction suggests that the amide substituent is important in relation to the extent of oxidation achieved, while the enantioselectivity of the reaction is determined by the nature of the sulfide moiety.

Upon scale up of this reaction to 2 mmol of the β-chloroacrylamide **1j**, the enantioselectivity was virtually identical to that obtained in the smaller scale (0.70 mmol) reactions. When the opposite (−)-enantiomer of diethyl tartrate was employed in preparing the catalyst complex, as expected the opposite enantiomer of the sulfoxide **2j** predominated in the product. Analysis of this material by chiral HPLC showed the material to again have 52% ee, with the (*R*)-enantiomer being predominant. As sulfoxide **2j** is an oil, recrystallisation of the product to increase the enantiomer ratio was not possible.

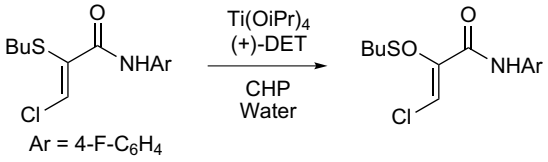
The effect of the sulfide substituent of the β-chloroacrylamide on the outcome of the asymmetric oxidation, using the Kagan procedure, has been shown above to be quite significant. As replacement of the arylthio substituent with *n*-butyl thio resulted in a significantly improved enantioselectivity, further investigation of *N*-alkyl thio derivatives was undertaken. The methanethio sulfides **1ai** and **1u** were investigated, as the optimum results in sulfur oxidation had been achieved with methyl aryl sulfides, while the *i*-butyl derivatives **1s** and **1aj** were explored to determine the impact of branching in the alkylthio chain on the enantioselective oxidation.

When the methanethio derivatives **1ai** and **1u** were subjected to standard Kagan oxidation conditions, a decrease in enantioselectivity was observed in comparison to the *n*-butylthio derivatives (Table 3, entries 11 and 12), while Kagan oxidation of the *i*-butyl sulfides **1s** and **1aj** led to recovery of the corresponding (*S*)-iso butyl sulfoxides **2s** and **2aj** with poor enantiomer ratios of 17% ee and 7% ee, respectively (Table 3, entries 13 and 14). Clearly, it can be seen that branching had a detrimental effect on the enantioselectivity, while the methanethio derivatives did not mimic methyl aryl sulfides.

In 1996, Kagan published a truly catalytic version of his chiral titanium derived catalyst for the asymmetric oxidation of sulfides to sulfoxides.[27] The complex employed differed from the original system in that water was replaced with 4 equiv of isopropanol, 1 equiv of 4 Å molecular sieves was added and the overall ratio of the catalyst complex to the sulfide was reduced from 2:1 to 0.1:1. Oxidation of **1a** and **1m** was attempted using this procedure. Oxidation of **1a** using this method resulted in poorer conversion to the sulfoxide **2a**, with a slight increase in the enantioselectivity to 15% ee (Table 3, entry 15). No oxidation occurred when **1m** was employed using this method.

In a 1995 paper, Kagan[28] explored the possibility of increasing the selectivity of the oxidation by varying parameters such as temperature, time, rate of addition and ageing of the catalyst complex. Up to this point, the optimum conditions as reported in an Organic Synthesis paper[26] had been employed. It was clear that in order to increase the selectivity of the reaction for the optimum substrate **1j**, we needed to further examine the oxidation conditions. To this end, a number of reactions were conducted, as outlined in Table 4, where temperature, the number of equivalents of the titanium complex and the rate of addition of the oxidant were examined.

Table 4
Optimisation of Kagan oxidation of **1j**



Conditions	Conversion[a] (%)	ee[b] (%)
Standard conditions	>95	53[d]
1:1:2:2:2 ratio of Ti/water/DET/sulfide/oxidant[c]		
Reagent prepared as described[c], CHP added in one lot at −20 °C		
CHP added in 6 portions over 1 h	>95	52
Full equivalent of titanium complex	>95	51
Full equivalent of Ti complex and CHP added in 6 portions over 1 h	>95	52
Reaction conducted at −50 °C for 18 h	30	37
Reaction conducted at 4 °C for 18 h	>95	40
Reaction conducted at room temperature for 18 h	>95	32
Standard conditions[c] on 2.00 mmol scale	>95	51
Standard conditions[c] using (−)-DET	>95	52[e]

[a] As estimated by ^{1}H NMR spectroscopy at 60 MHz in $CDCl_3$ of the crude reaction mixture.
[b] As estimated by chiral HPLC using a Chiralcel AS column at ambient temperature in 90:10 hexane/isopropanol, detection at 254 nm.
[c] As reported by Kagan et al.[26]
[d] The specific rotation of this sample was recorded; $[\alpha]_D^{20} = -98$ (*c* 1.3, DCM).
[e] As expected, the enantioselectivity in the sulfoxide was reversed; $[\alpha]_D^{20} = +94$ (*c* 1.7, DCM).

The conclusion, which can be drawn from these experiments, is that none of the modifications resulted in an improved enantioselectivity relative to the standard Kagan conditions. The addition of the oxidant, CHP, in 6 portions over 1 h, use of a full equivalent of the titanium complex and a combination of both gave material with effectively the same enantioselectivity. Only when the reaction was conducted at lower temperature (−50 °C) was less than complete conversion obtained and the slower rate of the reaction was accompanied by a reduction in enantioselectivity. Conducting the reaction at 4 °C or at room temperature also gave poorer enantioselectivity, suggesting that −20 °C is at or near the optimum temperature for the oxidation, as reported by Kagan.[26]

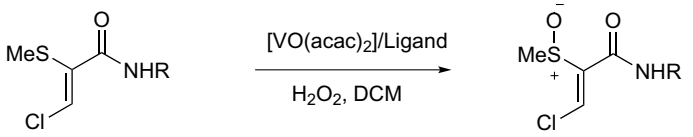
In conclusion, the optimum enantioselectivity achieved with the Kagan oxidation was 51% ee with the *n*-butyl thio derivative **2j**. Interestingly, only *N*-aryl amides undergo the oxidation. Enantioselectivity is enhanced by the presence of the *N*-4-fluoroaniline substituent.

2.3.2. Bolm oxidation

Asymmetric oxidation of the β-chloroacrylamides using the Bolm method was also explored. Initially, a number of reactions were carried out on the (*S*)-methyl derived β-chloroacrylamides, where the influences of temperature, scale and ligand were examined in detail (Table 5).

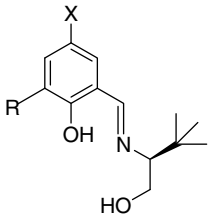
The initial reaction involved the oxidation of the (*S*)-methyl β-chloroacrylamide **1u** using the original Bolm conditions {1 mol %

Table 5
Bolm oxidation of the *S*-methyl β-chloroacrylamides

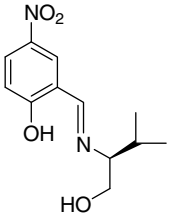


R=4-F-C_6H_4 **1u** **2u**
R=*n*-Bu **1v** **2v**
R=Bn **1w** **2w**

Entry	R	Ligand	Temperature (°C)	% Conversion[a]	Yield[b] (%)	Enantioselectivity[c] (% ee)
1	4-F–C_6H_4	**5a**	Ambient	72	51	45
2	4-F–C_6H_4	**5a**	0	100	70	71
3	4-F–C_6H_4	**5a**	−20	100	81	69
4	4-F–C_6H_4	**5a**	−30	100	73	61
5[d]	4-F–C_6H_4	**5a**	−20	100	81	71
6[e]	4-F–C_6H_4	**5a**	−20	100	82	53
7[e]	4-F–C_6H_4	**5a**	−20	100	85	62
8[e]	4-F–C_6H_4	**5a**	−20	100	82	63
9	4-F–C_6H_4	**5b**	Ambient	100	67	72
10	4-F–C_6H_4	**5b**	−20	60	41	60
11	4-F–C_6H_4	**5c**	Ambient	100	87	23
12	4-F–C_6H_4	**5d**	Ambient	95	66	71
13	4-F–C_6H_4	**5d**	−20	60	41	61
14	4-F–C_6H_4	**5e**	Ambient	95	62	66
15	4-F–C_6H_4	**5e**	−20	68	51	70
16	4-F–C_6H_4	**5f**	Ambient	85	71	70
17	4-F–C_6H_4	**5f**	−20	100	86	71
18	4-F–C_6H_4	**5g**	Ambient	100	82	70
19	4-F–C_6H_4	**5g**	−10	100	85	51
20	4-F–C_6H_4	**5h**	Ambient	47	30	36
21	4-F–C_6H_4	**5h**	0	45	32	30
22	4-F–C_6H_4	**5h**	−10	40	37	20
23	4-F–C_6H_4	**5h**	−20	51	32	71[g]
24	4-F–C_6H_4	**5i**	Ambient	44	32	24
25	4-F–C_6H_4	**5i**	0	40	30	34
26	4-F–C_6H_4	**5i**	−10	80	55	68
27	4-F–C_6H_4	**5i**	−20	32	24	22
28	4-F–C_6H_4	**5j**	Ambient	100	88	56
29	4-F–C_6H_4	**5j**	−20	100	87	56
30	Bn	**5a**	Ambient	62	50	30
31	Bn	**5a**	−10	100	85	61
32	Bn	**5a**	−20	100	82	59
33	*n*-Bu	**5a**	Ambient	40	31	35
34	*n*-Bu	**5a**	−20	100	72	71
35[f]	*n*-Bu	**5a**	−20	20	7	71
36	*n*-Bu	**5k**	−20	0	–	–



R=H, X=NO_2 **5a**
R=X=H **5b**
R=Bu^t, X=NO_2 **5c**
R=Me, X= H **5d**
R=H, X=Me **5e**
R=H, X=Bu^t **5f**
R=H, X = Cl **5g**
R=X=I **5h**
R=X=Br **5i**
R=X=Bu^t **5k**



5j

[a] Estimated from integration of ^{1}H NMR spectra of crude samples.
[b] Yields quoted are following chromatography.
[c] Enantiomer ratios were determined using chiral HPLC using IPA/hexane as mobile phase on a Chiralcel AS column detected at λ 254 nm.
[d] This reaction was carried out on a 1 g scale (4 mmol).
[e] This reaction was carried out on a 2.5 g scale. On this scale the enantioselectivity of the product was seen to decrease even when the hydrogen peroxide was added over 16 h using a syringe pump.
[f] This reaction was worked up after 2 h (16 h in all other cases).
[g] >98% ee was achieved on recrystallisation from 1:1 mixture of hexane/chloroform.

[$VO(acac)_2$], 1.5 mol % ligand, 1.1 equiv H_2O_2, rt, DCM} with ligand **5a**. Then, ^{1}H NMR spectroscopy of the crude reaction mixture showed 72% conversion of β-chloroacrylamide **1u** to the corresponding sulfoxide **2u**. Following chromatography, sulfoxide **2u** was isolated in 51% yield with 45% ee (Table 5, entry 1). Decreasing the temperature of the reaction increased the conversion (quantitative at −30 °C or 0 °C) and the ee of the resultant sulfoxide **2u**, with the optimum enantioselectivity obtained at −20/0 °C (Table

5, entries 1–4). This transformation was scaled up successfully from using 1 mmol (0.25 g) to 4 mmol (1.00 g) of β-chloroacrylamide **1u**, but when increased to 10 mmol, the enantioselectivity decreased slightly to 62% or 63% ee, even when the oxidant was added slowly over 16 h. The conversion (100%), yield (81%) and the enantioselectivity (71% ee) obtained on a 4 mmol scale were consistent with those obtained on a 1 mmol scale (Table 5, entry 3 vs entry 5).

Since the enantioenriched (*S*)-methyl sulfoxide **2u** is a solid, an enhancement of the enantiomeric ratio by recrystallisation was attempted. Following slow (ca. 2 weeks) vapour diffusion recrystallisation from chloroform/hexane (1:1), a number of distinct crystals were obtained. Analysis of the resulting crystals and the mother liquor showed that individual enantiopure crystals of **2u** could be obtained but this method was not practical for producing synthetically useful amounts of enantiopure **2u**.

The (*S*)-absolute stereochemistry was determined by single crystal X-ray diffraction on an enantiopure crystal of **2u** (see Fig. 2). Critically, chiral LC demonstrated that this is the major enantiomer formed in the Bolm oxidation using the (*S*)-ligand. The absolute stereochemistry of the other sulfoxide derivatives was assigned by analogy on the basis of similar profiles in chiral LC and direction of specific rotations. The (*S*)-sulfoxides **2u**–**w** are formed selectively using the (*S*)-ligand in the Bolm oxidation. This is consistent with the stereoselectivity, which has been reported previously.[21,23,29]

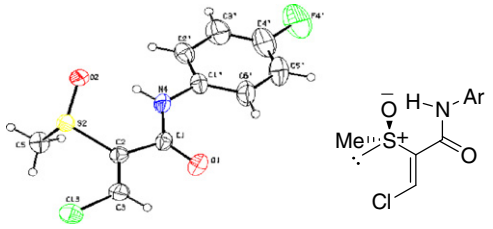


Figure 2. A view of **2u** showing the structure and absolute stereochemistry. Anisotropic displacement parameters are drawn at the 30% probability level.

An investigation on the impact of the nature of the ligand on the Bolm oxidation of β-chloroacrylamide **1u** was then explored. Ligands **5a**–**k** were selected for investigation based on the literature reports by Bolm and others.[21,30] For the Bolm oxidation of alkyl aryl sulfides, **5h** has proven to be highly enantioselective, with 97% ee achieved for methyl naphthylsulfoxide.[30] Sulfide oxidation of **1u** was achieved with varying efficiency and enantioselectivity using ligands **5a**–**k**.

In conclusion, the temperature at which optimum selectivity occurs varies depending on the structure of the ligand. For example, with **5h** 71% ee was achieved at −20 °C (Table 5, entry 23), while with **5d** similar enantioselectivity was achieved at room temperature (Table 5, entry 12).

Replacement of the *t*-Bu substituent with *i*-Pr in **5j** resulted in efficient oxidation but decreased enantioselectivity relative to **5a** (56% ee vs 71% ee), highlighting the importance of a bulky substituent at this position. The presence of a H, Me or halo substituent at C-3 of the ligand is readily tolerated, but the introduction of a *t*-Bu group at this position results in a dramatic decrease in enantioselectivity (Table 5, entry 11). The presence of a H, Me, *t*-Bu, NO_2 or halo substituent at C-5 can be tolerated. The optimum enantioselectivity with each of the ligands was 70–71% ee.

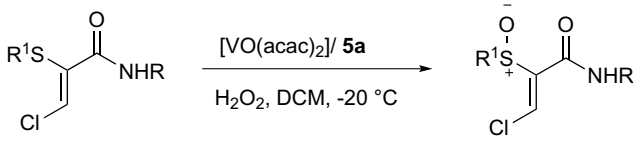
The impact of the electronic effect of the amide substituent was next investigated by replacing the *N*-aryl substituent with *N*-benzyl **1w** or *N*-alkyl **1v** using ligands **5a** and **5u**. In both oxidations with ligand **5a**, the conversions and the ee's tended to increase when decreasing the reaction temperature (Table 5, entries 30–35). Optimum enantioselectivities of 61% ee (**2w**) and 71% ee (**2v**) were achieved. When the oxidation of **1v** was repeated and worked up after 2 h compared to 16 h under standard conditions, the extent of conversion was significantly decreased, but critically the enantioselectivity of oxidation to the sulfoxide was unaffected, indicating that it is not affected by progress of the reaction.

The Bolm oxidation of β-chloroacrylamide **1v** was also conducted in the presence of ligand **5k** at −20 °C. Interestingly, the presence of the bulky *t*-butyl groups on ligand **5k** inhibited the reaction completely (Table 5, entry 36).

To investigate the impact of substrate structure on the Bolm oxidation, a study of the Bolm oxidation of β-chloroacrylamides **1s**, **1ak** and **1t** under various reaction conditions was then conducted, and the optimum results of this work are outlined in Table 6. The results obtained are similar to those obtained with the methanethio derivatives, with 67–71% ee achieved, indicating that increasing the steric hindrance adjacent to the sulfur does not noticeably affect the enantioselectivity.

In conclusion, the outcome of the Bolm oxidation of the β-chloroacrylamides is rather insensitive to variation of the sulfide structure and the electronic properties of the ligand. The only significant effect observed during the course of this work was steric, that is, there was a dramatic fall off in the enantioselectivity of the sulfide oxidation in all cases when ligands **5c** and **5k**, both bearing a *t*-butyl group on the C-3 position of the aromatic ring, were employed in the Bolm oxidation of the β-chloroacrylamides (see Fig. 3). Interestingly, this contrasts with Bolm's results where he described higher enantioselectivity using ligand **5c** bearing the 3-*t*-butyl group compared to the less sterically hindered ligand **5a**.[21] However, in 2005, Zeng reported that ligands derived from 3,5-di-*tert*-butylsalicylaldehyde gave lower enantioselectivities in the sulfoxidation of thioanisole than those derived from less sterically

Table 6
Bolm oxidation of β-chloroacrylamides **1s**, **1ak** and **1t**



R^1	R	Sulfoxide	Eq. H_2O_2	% Conversion[a]	% Yield[b]	Enantioselectivity (% ee)[c]
i-Bu	4-F–C_6H_4	**2s**	2.0	73	59	67
i-Bu	Tol	**2ak**	1.1	91	72	71
i-Pr	4-F–C_6H_4	**2t**	1.1	100	76	71

[a] Estimated from integration of ^{1}H NMR spectra of crude samples.
[b] Yields quoted are following chromatography.
[c] Enantiomeric ratios were determined by chiral HPLC using IPA/hexane as mobile phase on a Chiralcel AS column detected at λ 254 nm.

hindered salicylaldehyde.[31] In general, the maximum enantioselectivity obtained for the sulfoxides was ca. 70% ee. However, the temperature at which this maximum occurred varied depending on the sulfide and ligand employed. Also, the predominant enantiomer in all cases was identified by X-ray crystallography and chiral HPLC as the (*S*)-enantiomer, when the (*S*)-ligand was employed.

The nature of the catalytically active species has already been discussed extensively by Bryliakov,[29] Zeng,[31] Bolm[32–34] and Ellman.[35] It is clear that the presence of a *t*-Bu group at C-3 hinders approach of the sulfide to the reacting vanadium complex (Fig. 4), thereby allowing achiral oxidation to compete with the enantioselective vanadium catalysed oxidation.

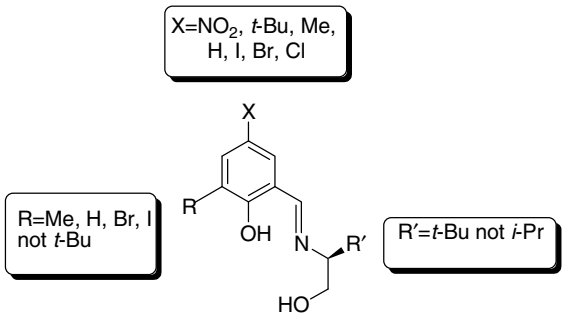


Figure 3.

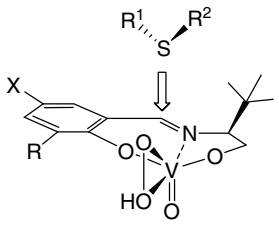
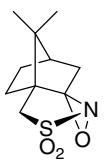


Figure 4.

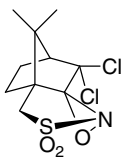
Following the development of the vanadium catalysed process, Bolm has reported that aryl alkyl sulfides can be rapidly oxidised to give chiral sulfoxides with enantioselectivities up to 90% ee using an iron catalyst formed in situ from $Fe(acac)_3$ and Schiff base ligands **5g**–**5i**.[36] Significantly, Bolm has reported improved stereoselectivities in the iron catalysed sulfide oxidation in the presence of additives such as substituted benzoic acids, although the use of these additives was not explored in this work.[37] Accordingly, the iron catalysed asymmetric oxidation of sulfide **1u** was explored using ligands **5a**, **5g**–**5i** as outlined in Table 7.

The efficiency and the enantioselectivity of the oxidation to form the methyl sulfoxide **2u** are lower than the results obtained with the vanadium based system. Decreasing the reaction temperature appears to have a positive impact on the enantioselectivity of sulfoxide **2u**, albeit with associated decrease in conversion (Table 7, entry 3).

The Page oxidation[38] (with oxaziridines **6a** and **6b** and sulfides **1a** and **1j**) and enzymatic oxidation[39] (with **1a** and chloroperoxidase, CPO from *Calsariomyces fumago*) were also explored. However, no conversion to the sulfoxides was observed under these conditions.

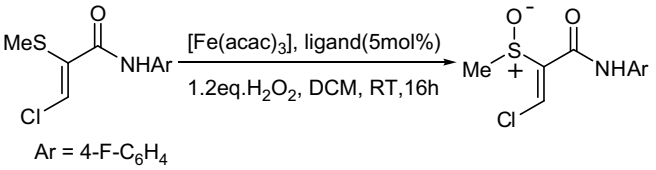


6a



6b

Table 7
$Fe(acac)_3$ catalysed Bolm oxidation



Ar = 4-F-C_6H_4

Entry	Ligand	Temperature (°C)	% Conversion[a]	Yield[b] (%)	Enantioselectivity[c] (% ee)
1	**5h**	Ambient	44	28	23
2	**5i**	Ambient	41	26	30
3	**5i**	−10	21	19	38
4	**5g**	Ambient	42	31	14
5	**5a**	Ambient	46	34	17

[a] Estimated from integration of ^1H NMR spectra of crude samples.
[b] Yields quoted are following chromatography.
[c] Enantiomeric ratios were determined using chiral HPLC using IPA/hexane as mobile phase on a Chiralcel AS column detected at λ 254 nm. As in the vanadium system, the (*S*)-enantiomer was obtained when the (*S*)-ligand was employed.

3. Conclusion

Enantioselective oxidation of the β-chloroacrylamides to the analogous sulfoxides can be achieved using the Kagan oxidation with titanium catalysis or the Bolm oxidation with vanadium or iron based systems. Enantioselectivities of up to 71% ee were obtained across a range of derivatives using the vanadium catalyst with Schiff base ligands. Investigation of the synthetic utility of the resulting highly functionalised sulfoxides as Michael acceptors, dienophiles and dipolarophiles is currently underway in our laboratory.

4. Experimental

All solvents were distilled prior to use as follows: dichloromethane was distilled from phosphorous pentoxide and ethyl acetate was distilled from potassium carbonate, ethanol and methanol were distilled from magnesium in the presence of iodine. Organic phases were dried using anhydrous magnesium sulfate. All commercial reagents, including *N*-chlorosuccinimide, were used without further purification.

^1H (300 MHz) and ^{13}C (75.5 MHz) NMR spectra were recorded on a Bruker (300 MHz) NMR spectrometer. ^1H (270 MHz) and ^{13}C (67.8 MHz) NMR spectra were recorded on a Jeol GSX (270 MHz) NMR spectrometer. ^1H (60 MHz) NMR spectra were recorded on a Jeol PMX-60SI spectrometer. All spectra were recorded at room temperature (~20 °C) in deuterated chloroform ($CDCl_3$) unless otherwise stated using tetramethylsilane (TMS) as an internal standard. Chemical shifts were expressed in parts per million (ppm) and coupling constants in Hertz (Hz).

Elemental analyses were performed by the Microanalysis Laboratory, National University of Ireland, Cork, using a Perkin–Elmer 240 elemental analyser. Melting points were carried out on a uni-melt Thomas Hoover Capillary melting point apparatus. Mass spectra were recorded on a Kratos Profile HV-4 double focusing high resolution mass spectrometer (EI), a Waters/Micromass LCT Premier Time of Flight spectrometer (ESI) and a Waters/Micromass Quattro Micro triple quadrupole spectrometer (ESI). Infrared spectra were recorded as potassium bromide (KBr) discs for solids or thin films on sodium chloride plates for oils on a Perkin–Elmer Paragon 1000 FT-IR spectrometer.

Thin layer chromatography (TLC) was carried out on precoated silica gel plates (Merck 60 PF_{254}). Column chromatography was performed using Merck Silica Gel 60. Visualisation was achieved by UV (254 nm) light detection, iodine staining, vanillin staining and ceric sulfate staining.

4.1. Single crystal X-ray crystallographic analysis

Data were collected on a Nonius MACH3 diffractometer using Mo-Kα graphite monochromated radiation, $\lambda = 0.7107$ Å, and corrected for Lorentz and polarisation effects. The structures were solved by direct methods and refined by full-matrix least-squares using all F^2 data. The SHELXS, SHELXL-97[40] and PLATON[41] suite of programs were used. All non-hydrogen atoms were refined with anisotropic displacement factors. The hydrogen atoms were placed in calculated positions and allowed to ride on the parent atom. The (*S*)-enantiomer for **2u** was unambiguously confirmed using the Flack parameter. Full structural data have been deposited at the Cambridge Crystallographic Data Centre. CCDC reference numbers 676357 and 676358.

4.2. *N*-4′-Methylphenyl-*Z*-3-chloro-2-(benzenesulfinyl)-propenamide 2a

A solution of Oxone® (6.08 g, 9.88 mmol) in water (30 mL) was added dropwise to a stirred solution of *N*-4′-methylphenyl-*Z*-3-chloro-2-(phenylthio)-propenamide **1a** (1.50 g, 4.94 mmol) in acetone (120 mL) at room temperature. A colourless precipitate formed immediately. The reaction mixture was stirred for 2 h and then checked for completion by TLC. Water (200 mL) was added and the aqueous solution extracted with DCM (3 × 75 mL). The combined extracts were washed with water (2 × 100 mL) and brine (100 mL), dried and concentrated to give **2a**. The crude product was purified by chromatography on silica gel using ethyl acetate/hexane (20:80) as eluent to give the sulfoxide **2a** (1.52 g, 96%) as a colourless solid; mp 128–129.5 °C; $C_{16}H_{14}NClO_2S$ requires C, 60.09; H, 4.41; N, 4.38; Cl, 11.09; S, 10.03. Found: C, 60.40; H, 4.61; N, 4.17; Cl, 11.53; S, 9.80. ν_{max}/cm^{-1} (KBr) 1671 (CO), 1612, 1555, 1512, 1319, 1034 (SO), 726; δ_H 2.30 (3H, s, Ar-CH_3), 7.08–7.18 (2H, m, ArH), 7.39–7.56 (5H, m, ArH), 7.67–7.79 (2H, m, ArH), 7.83 (1H, s, CHCl=), 10.37 (1H, br s, NH); δ_C 20.80 (*C*H_3Ar), 120.69 (aromatic CH), 124.14 (aromatic CH), 129.50 (aromatic CH), 129.73 (aromatic CH), 131.84 (aromatic CH), 134.63 (quaternary aromatic or SC=), 134.67 (quaternary aromatic or SC=), 137.40 (*C*HCl=), 138.77 (quaternary aromatic C or SC=), 141.07 (quaternary aromatic C or SC=), 158.12 (CO); MS *m*/*z* 319 (M^+, 84%), 226 (47), 213 (12, M^+-NHTol), 134 (73, $[PhS{=}C{=}CH]^+$), 125 (100, $[SOPh]^+$), 77 (95); isotopic Cl pattern observed; 319, 321 (3:1 ratio $^{35}Cl/^{37}Cl$). Found (HRMS, EI) *m*/*z* 319.0377. $C_{16}H_{14}N^{35}ClO_2S$ requires 319.0434.

4.3. *N*-Benzyl-*Z*-3-chloro-2-(benzenesulfinyl)propenamide 2b

This was prepared using the procedure described for **2a** using Oxone® (6.09 g, 9.9 mmol) in water (35 mL) to a stirred solution of β-chloroacrylamide **1b** (1.00 g, 3.3 mmol) in acetone (100 mL) at 0 °C. The crude product was purified by chromatography on silica gel using ethyl acetate/hexane (20:80) as eluent to give sulfoxide **2b** (1.03 g, 98%) as a colourless solid; mp 80–82 °C; $C_{16}H_{14}NClO_2S$ requires C, 60.09; H, 4.41; N, 4.38; Cl, 11.09; S, 10.03. Found: C, 59.65; H, 4.56; N, 4.32; Cl, 11.89; S, 10.22. ν_{max}/cm^{-1} (KBr) 1659 (CO), 1574, 1028 (SO), 715; δ_H 4.23–4.37 (1H, A of ABX, J_{AX} 5, J_{AB} 15, NCH_2), 4.55–4.68 (1H, B of ABX, J_{BX} 7, NCH_2), 7.02–7.70 (10H, m, ArH), 7.78 (1H, s, CHCl=), 9.73 (1H, br s, NH); δ_C 43.27 (CH_2Ph), 124.13 (aromatic CH), 127.42 (aromatic CH), 127.64 (aromatic CH), 128.31 (aromatic CH), 128.85 (aromatic CH), 131.58 (aromatic CH), 137.37 (*C*HCl=), 138.73 (quaternary aromatic C or SC=), 140.95 (quaternary aromatic C or SC=), 160.51 (CO); MS *m*/*z* 319 (M^+, 9%), 284 (4, M^+-Cl), 194 (17, M^+-SOPh), 134 (97, $[PhS{=}C{=}CH]^+$), 91 (100, $[PhCH_2]^+$), 77 (65); isotopic Cl pattern observed; 319, 321 (3:1 ratio $^{35}Cl/^{37}Cl$). Found (HRMS, EI) 319.0438. $C_{16}H_{14}N^{35}ClO_2S$ requires 319.0434.

Note: Two quaternary carbon signals were observed for three carbons (2 quaternary aromatic carbons and SC=).

4.4. *N*-Isopropyl-*Z*-3-chloro-2-(benzenesulfinyl)propenamide 2c

This was prepared using the procedure described for **2a** using Oxone® (9.63 g, 15.66 mmol) in water (50 mL) and *N*-*i*-propyl-*Z*-3-chloro-2-(phenylthio)propenamide **1c** (2.00 g, 7.83 mmol) in acetone (160 mL) at room temperature. The crude product was purified by chromatography on silica gel using ethyl acetate/hexane (20:80) as eluent to give the sulfoxide **2c** (2.08 g, 98%) as a white solid; mp 100–102 °C; $C_{12}H_{14}NClO_2S$ requires C, 53.03; H, 5.19; N, 5.16; Cl, 13.04; S, 11.80. Found: C, 52.60; H, 5.52; N, 5.15; Cl, 13.28; S, 11.39. ν_{max}/cm^{-1} (KBr) 3294 (br, NH), 1627 (CO), 1540, 1082, 1055; δ_H 1.02 (3H, d, *J* 6, one of $CH(CH_3)_2$), 1.18 (3H, d, *J* 6, one of $CH(CH_3)_2$), 3.89–4.09 (1H, m, NCH), 7.42–7.68 (5H, m, ArH), 7.71 (1H, s, CHCl=), 8.19 (1H, br s, NH); δ_C 22.29 (both of $CH(CH_3)_2$), 41.47 (NCH), 124.03 (aromatic CH), 129.20 (aromatic CH), 131.49 (aromatic CH), 136.83 (*C*HCl=), 138.90 (quaternary aromatic or SC=), 141.10 (quaternary aromatic or SC=), 159.29 (CO).

4.5. *N*-Ethyl-*Z*-3-chloro-2-(benzenesulfinyl)propenamide 2d

This was prepared using the procedure described for sulfoxide **2a** using *N*-ethyl-*Z*-3-chloro-2-(phenylthio)propenamide **1d** (slightly impure) (2.18 g, 9.05 mmol) in acetone (220 mL) and Oxone® (16.69 g, 27.15 mmol) in water (96 mL) to give the crude sulfoxide. Purification by chromatography on silica gel using ethyl acetate/hexane (70:30) as eluent gave the sulfoxide **2d** (1.32 g, 57%) as a colourless solid; mp 75–78 °C; $C_{11}H_{12}NClO_2S$ requires C, 51.26; H, 4.69; N, 5.44; Cl, 13.75; S, 12.44. Found: C, 51.13; H, 4.68; N, 5.41; Cl, 14.23; S, 12.55. ν_{max}/cm^{-1} (KBr) 3254 (NH), 1664 (CO), 1568, 1541, 1030, 758; δ_H 1.08 (3H, t, *J* 7, $-CH_3$), 3.17–3.42 (2H, m, NCH_2), 7.48–7.72 (5H, m, ArH), 7.73 (1H, s, CHCl=), 8.33 (1H, br s, NH); δ_C 14.37 ($-CH_3$), 34.17 (NCH_2), 124.07 (aromatic CH), 129.07 (aromatic CH), 131.59 (aromatic CH), 136.85 (*C*HCl=), 138.79, 114.07 (2 signals for 3 carbons: 2 quaternary aromatics and SC=), 160.17 (CO); MS *m*/*z* 257 (M^+, 80%), 164 (47), 134 (50, $[PhS{=}C{=}CH]^+$), 125 (97, $[SOPh]^+$), 77 (93), 44 (100); isotopic Cl pattern observed; 257, 259 (3:1 ratio $^{35}Cl/^{37}Cl$); Found (HRMS, EI) *m*/*z* 257.0278. $C_{11}H_{12}N^{35}ClO_2S$ requires 257.0277.

4.6. *N*-*n*-Butyl-*Z*-3-chloro-2-(benzenesulfinyl)propenamide 2e

This was prepared using the procedure described for sulfoxide **2a** using *N*-*n*-butyl-*Z*-3-chloro-2-(phenylthio)propenamide **1e** (1.50 g, 5.57 mmol) in acetone (120 mL) and Oxone® (6.85 g, 11.14 mmol) in water (35 mL) for 2 h to give **2e**. The crude product was purified by chromatography on silica gel using ethyl acetate/hexane (20:80) as eluent to give the sulfoxide **2e** (1.56 g, 98%) as a clear oil; $C_{13}H_{16}NClO_2S$ requires C, 54.63; H, 5.64; N, 4.90; Cl, 12.41; S, 11.22. Found: C, 54.28; H, 5.60; N, 5.00; Cl, 12.62; S, 10.78. ν_{max}/cm^{-1} (film) 3283 (br, NH), 1660 (CO), 1538, 1329, 1160, 1086; δ_H 0.86 (3H, t, *J* 7, $-CH_3$), 1.08–1.51 (4H, m, $-CH_2-CH_2-$), 3.08–3.36 (2H, m, NCH_2), 7.39–7.66 (5H, m, ArH), 7.74 (1H, s, CHCl=), 8.31 (1H, br s, NH); δ_C 13.52 (CH_3, $-CH_3$), 19.77 (CH_2, $-CH_2$-3′), 31.14 (*C*H_2, CH_2-2′), 38.95 (CH_2, NCH_2-), 124.03

(*C*H, aromatic CH), 129.20 (*C*H, aromatic CH), 131.49 (*C*H, aromatic CH), 136.90 (*C*H, CHCl=), 138.81 (quaternary aromatic or SC=), 141.12 (quaternary aromatic or SC=), 160.28 (CO); MS *m*/*z* 285 (M^+, 36%), 250 (4, M^+-Cl), 242 (20), 213 (9, M^+-NHBu^n), 155 (100), 125 (65, $[SOPh]^+$), 77 (85); isotopic Cl pattern observed; 285, 287 (3:1 ratio $^{35}Cl/^{37}Cl$); Found (HRMS, EI) *m*/*z* 285.0583 $C_{13}H_{16}N^{35}ClO_2S$ requires M^+ 285.0590.

4.7. *N*-2′-Propenyl-*Z*-3-chloro-2-(benzenesulfinyl)propenamide 2f

This was prepared using the procedure described for sulfoxide **2f** using *N*-2′-propenyl-*Z*-3-chloro-2-(phenylthio)propenamide **1f** (1.50 g, 5.92 mmol) in acetone (120 mL) and Oxone® (7.28 g, 11.84 mmol) in water (36 mL) for 2 h to give **2f**. The crude product was purified by chromatography on silica gel using ethyl acetate/hexane (20:80) as eluent to give the sulfoxide **2f** (1.56 g, 98%) as a clear oil, which solidified on standing; mp 87–89 °C; $C_{12}H_{12}NClO_2S$ requires C, 53.43; H, 4.48; N, 5.19; Cl, 13.14; S, 11.89. Found: C, 53.37; H, 4.73; N, 5.21; Cl, 13.50; S, 11.38. ν_{max}/cm^{-1} (film) 3283 (br, NH), 1662 (CO), 1542, 1329, 1167, 1034; δ_H 3.73–4.00 (2H, m, NCH_2), 5.00–5.15 (2H, m, $=CH_2$), 5.63–5.82 (1H, m, CH=), 7.46–7.71 (5H, m, ArH), 7.76 (1H, s, CHCl=), 8.48 (1H, br s, NH); δ_C 41.68 (CH_2, NCH_2), 116.46 (CH_2, $=CH_2$), 124.14 (*C*H, aromatic CH), 129.07 (*C*H, aromatic CH), 129.26 (*C*H, aromatic CH), 131.64 (*C*H, CHCl= or CH=), 132.83 (*C*H, CHCl= or CH=), 138.83 (*C*, quaternary aromatic or SC=), 141.10 (*C*, quaternary aromatic or SC=), 160.26 (CO).

4.8. *Z*-3-Chloro-2-(benzenesulfinyl)propenamide 2g

This was prepared using the procedure described for sulfoxide **2a** using *Z*-3-chloro-2-(phenylthio)propenamide **1g** (0.50 g, 2.34 mmol) in acetone (40 mL) and Oxone® (2.88 g, 4.68 mmol) in water (14 mL) for 2 h to give **2g**. The crude product was purified by chromatography on silica gel using ethyl acetate/hexane (20:80) as eluent to give the sulfoxide **2g** (0.49 g, 92%) as a colourless solid; mp 157–161 °C (with decomposition); $C_9H_8NClO_2S$ requires C, 47.06; H, 3.51; N, 6.10; Cl, 15.43; S, 13.96. Found: C, 47.19; H, 3.38; N, 6.20; Cl, 15.94; S, 13.48. ν_{max}/cm^{-1} (KBr) 1678 (CO), 1566, 1031; δ_H 6.00 (1H, br s, one of NH_2), 7.42–7.72 (5H, m, ArH), 7.80 (1H, s, CHCl=), 8.26 (1H, br s, one of NH_2); δ_C 124.50 (aromatic CH), 129.95 (aromatic CH), 132.02 (aromatic CH), 138.29 (*C*HCl=), 139.41 (quaternary aromatic or SC=), 141.32 (quaternary aromatic or SC=), 162.00 (CO); MS *m*/*z* 229 (M^+, 64%), 194 (3, M^+-Cl), 125 (100, $[SOPh]^+$), 94 (55), 77 (70), 51 (64); isotopic Cl pattern observed; 229, 231 (3:1 ratio $^{35}Cl/^{37}Cl$); Found (HRMS, EI) *m*/*z* 228.9950. $C_9H_8N^{35}ClO_2S$ requires 228.9964.

4.9. *N*-4′-Fluorophenyl-*Z*-3-chloro-2-(benzenesulfinyl)-propenamide 2h

This was prepared using the procedure described for sulfoxide **2a** using *N*-4′-fluorophenyl-*Z*-3-chloro-2-(phenylthio)-propenamide **1h** (1.00 g, 3.25 mmol) in acetone (80 mL) and Oxone® (4.00 g, 6.50 mmol) in water (20 mL) for 4 h to give **2h**. The crude product was purified by chromatography on silica gel using ethyl acetate/hexane (20:80) as eluent to give the sulfoxide **2h** (1.09 g, 95%) as a colourless solid; mp 99–101 °C; $C_{15}H_{11}NClFO_2S$ requires C, 55.64; H, 3.42; N, 4.33; Cl, 10.95; F, 5.87; S, 9.90. Found: C, 56.00; H, 3.69; N, 4.31; Cl, 11.25; F, 5.75; S, 9.65. ν_{max}/cm^{-1} (KBr) 1675 (CO), 1621, 1574, 1508, 1216, 1029, 721; δ_H 7.00 (2H, overlapping dd, *J* 9, 9, C-3 ArH), 7.48–7.58 (5H, m, ArH), 7.67–7.73 (2H, m, ArH), 7.83 (1H, s, CHCl=), 10.43 (1H, br s, NH); δ_C 115.65 (d, $^3J_{CF}$ 23, aromatic CH, ArC-3), 122.29 (d, $^2J_{CF}$ 9, aromatic CH, ArC-2), 124.11 (aromatic CH), 129.79 (aromatic CH), 131.95 (aromatic CH), 133.18 (quaternary aromatic), 137.82 (*C*HCl=), 138.48 (quaternary aromatic or SC=), 140.88 (quaternary aromatic or SC=), 157.88/161.47 (d, $^4J_{CF}$ 244, quaternary aromatic, ArC-4), 158.30 (CO); MS *m*/*z* 323 (M^+, 23%), 231 (25), 125 (50, $[SPh]^+$), 43 (100); isotopic Cl pattern observed; 323, 325 (3:1 $^{35}Cl/^{37}Cl$); Found (HRMS, EI) *m*/*z* 323.0176; $C_{15}H_{11}N^{35}ClFO_2S$ requires 323.0154.

Note: The β-chloroacrylamides of the (*n*-butylthio)propanamides are susceptible to over oxidation if exposed to Oxone for more than 2 h. As with the corresponding β-chloroacrylamides, these compounds should be stored under nitrogen in the freezer as they are rather labile. Decomposition of these compounds is evident by discolouration and the formation of a baseline spot on TLC.

4.10. Oxidation of *E*-1i to the sulfoxide 2i

A solution of Oxone® (1.02 g, 1.66 mmol) in water (5 mL) was added dropwise to a stirred solution of β-chloroacrylamide ***E*-1i** (200 mg, 0.83 mmol) in acetone (16 mL) at room temperature. The reaction mixture was stirred at room temperature for 14 h, then water (25 mL) was added and the aqueous layer extracted with DCM (3 × 20 mL). The combined extracts were washed with water (2 × 25 mL) and brine (40 mL), dried and concentrated at reduced pressure to give sulfoxide **2i** (210 mg, 98%) as a clear oil, which solidified on standing to give a colourless solid, which required no further purification; mp 96–98 °C; $C_{11}H_{12}NClO_2S$ requires C, 51.26; H, 4.69; N, 5.44; Cl, 13.75; S, 12.44. Found: C, 51.37; H, 4.49; N, 5.36; Cl, 13.29; S, 12.14. ν_{max}/cm^{-1} (KBr) 1648 (CO), 1560, 1086, 740; δ_H 2.88 (3H, s, one of $N(CH_3)_2$), 3.03 (3H, s, one of $N(CH_3)_2$), 6.74 (1H, s, CHCl=), 7.48–7.60 (3H, m, ArH), 7.74–7.86 (2H, m, ArH); δ_C 35.19 (one of $N(CH_3)_2$), 38.92 (one of $N(CH_3)_2$), 124.86 (aromatic CH), 126.01 (aromatic CH), 128.78 (aromatic CH), 131.66 (*C*HCl=), 141.78 (quaternary aromatic or SC=), 145.45 (quaternary aromatic or SC=), 161.18 (CO); MS *m*/*z* 258 (M^++1, 49%), 223 (46, 258-Cl), 175 (50), 126 (98), 78 (100), 73 (99).

4.11. *N*-4′-Fluorophenyl-*Z*-3-chloro-2-(*n*-butylsulfinyl)-propenamide 2j

This was prepared using the procedure described for sulfoxide **2a** using *N*-4′-fluorophenyl-*Z*-3-chloro-2-(*n*-butylthio)propenamide **1j** (1.00 g, 3.48 mmol) in acetone (80 mL) and Oxone® (4.28 g, 6.96 mmol) in water (22 mL) for 90 min to give **2j**. The crude product was purified by chromatography on silica gel using ethyl acetate/hexane (15:85) as eluent to give the sulfoxide **2j** (1.01 g, 95%) as a clear oil; $C_{13}H_{15}NClFO_2S$ requires C, 51.39; H, 4.98; N, 4.61; Cl, 11.67; F, 6.25; S, 10.55. Found: C, 51.49; H, 5.14; N, 4.58; Cl, 11.25; F, 6.44; S, 10.77. ν_{max}/cm^{-1} (film) 1676 (CO), 1574, 1510, 1224, 1017; δ_H 1.00 (3H, t, *J* 7, CH_3-4′), 1.45–1.62 (2H, m, CH_2-3′), 1.72–1.89 (2H, m, CH_2-2′), 2.90–3.05 (1H, m, one of SCH_2), 3.12–3.25 (1H, m, one of SCH_2), 7.02 (2H, overlapping dd, *J* 8, 8, C-3 ArH), 7.53–7.63 (2H, m, C-2 ArH), 7.80 (1H, s, CHCl=), 10.67 (1H, br s, NH); δ_C 13.43 (CH_3, CH_3-4′), 21.66 (CH_2, CH_2-3′), 24.27 (CH_2, CH_2-2′), 52.93 (CH_2, $SOCH_2$), 115.78 (*C*H, d, $^3J_{CF}$ 22, aromatic CH, ArC-3), 122.38 (*C*H, aromatic CH, ArC-2), 133.31 (*C*, quaternary aromatic or SC=), 136.12 (*C*, quaternary aromatic or SC=), 136.30 (*C*H, CHCl=), 157.79/161.40 (*C*, d, $^4J_{CF}$ 245, quaternary aromatic, ArC-4), 158.61 (CO); 303 (M^+, 35%), 268 (12, M^+-Cl), 247 (40), 164 (20), 149 (10, $M^+-CONHAr-O$), 136 (58), 111 (80), 57 (100); isotopic Cl pattern observed; 303, 305 (3:1 $^{35}Cl/^{37}Cl$); Found (HRMS, EI) *m*/*z* 303.0463; $C_{13}H_{15}N^{35}ClFO_2S$ requires 303.0496.

4.12. *N*-*n*-Butyl-*Z*-3-chloro-2-(butylsulfinyl)propenamide 2k

This was prepared following the procedure described for sulfoxide **2a** using *N*-*n*-butyl-*Z*-3-chloro-2-(butylthio)propenamide **1k**

(0.54 g, 2.2 mmol) in acetone (40 mL) and Oxone® (2.68 g, 4.4 mmol) in water (3 mL) for 2 h to give sulfoxide**1k**. Following purification by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 2–5% ethyl acetate), the pure sulfoxide **1k** (0.43 g, 80%) was isolated as a clear oil; ν_{max}/cm^{-1} (film) 3222 (NH), 1671 (CO), 1574 (NH bend), 1466, 1403 (CN stretch), 1025 (SO); δ_H (300 MHz) 0.91–1.00 [6H, m, C(4′)H_3 and C(4″)H_3], 1.25–1.77 [8H, m, C(3′)H_2, C(3″)H_2, C(2′)H_2 and C(2″)H_2], 2.89–2.92 (1H, m, one of SCH_2), 3.06–3.11 (1H, m, one of SCH_2), 3.34–3.37 (2H, m, NCH_2), 7.67 [1H, s, C(3)HCl=], 8.59 (1H, br s, NH); δ_C (75.5 MHz) 14.0 [CH_3, C(4′)H_3 or C(4″)H_3], 14.1 [CH_3, C(4′)H_3 or C(4″)H_3], 20.6 [CH_2, C(3′)H_2 or C(3″)H_2], 22.2 [CH_2, C(3′)H_2 or C(3″)H_2], 24.9 [CH_2, C(2′)H_2 or C(2″)H_2], 31.6 [CH_2, C(2′)H_2 or C(2″)H_2], 39.6 [CH_2, $C$$H_2$N], 53.1 ($CH_2$, $C$$H_2$S), 135.9 [CH, C(3)HCl=], 136.9 [C, C(2)S], 161.3 (C, CO).

4.13. *N*-Benzyl-*Z*-3-chloro-2-(*n*-butylsulfinyl)propenamide 2l

This was prepared following the procedure described for sulfoxide **2a** using *N*-benzyl-*Z*-3-chloro-2-(*n*-butylthio)propenamide **1l** (1.00 g, 3.53 mmol) in acetone (80 mL) and Oxone® (4.34 g, 7.06 mmol) in water (22 mL) for 2 h to give crude sulfoxide **2l** (1.06 g, quantitative). Purification by chromatography on silica gel using ethyl acetate/hexane (gradient elution 10–30% ethyl acetate) as eluent gave *N*-benzyl-*Z*-3-chloro-2-(*n*-butylsulfinyl)propenamide **2l** (0.93 g, 80%) as a clear oil; $C_{14}H_{18}NClO_2S$ requires C, 56.08; H, 6.05; N, 4.67; Cl, 11.82; S, 10.69. Found: C, 55.87; H, 6.19; N, 4.47; Cl, 11.69; S, 10.88. ν_{max}/cm^{-1} (film) 3252 (br NH), 1670 (CO), 1573, 1024 (SO), 699; δ_H 0.93 (3H, t, *J* 7, –CH_3-4′), 1.34–1.54 (2H, m, –CH_2-3′), 1.58–1.84 (2H, m, –CH_2-2′), 2.80–2.94 (1H, m, one of SOCH_2), 3.00–3.14 (1H, m, one of SOCH_2), 4.42–4.64 (2H, sym. m, NCH_2Ph), 7.18–7.40 (5H, m, ArH), 7.71 (1H, s, CHCl=), 9.03 (1H, br s, NH); δ_C 13.41 (CH_3, CH_3), 21.72 (CH_2, CH_2-3′), 24.16 (CH_2, CH_2-2′), 43.37 (CH_2, NCH_2Ph), 52.67 (CH_2, SOCH_2), 127.41 (CH, aromatic CH), 127.74 (CH, aromatic CH), 128.74 (CH, aromatic CH), 135.75 (CH, CHCl=), 136.70 (*C*, quaternary aromatic C or SOC=), 137.62 (quaternary aromatic C or SOC=), 161.00 (CO); MS *m*/*z* 299 (M^+, 1%), 264 (21, M^+–Cl), 194 (11, M^+–SOBu^n), 158 (45, M^+–SOBu^n–HCl), 91 (100, $[PhCH_2]^+$), 77 (36); isotopic Cl pattern observed on expansion; 299, 301 (3:1 ratio $^{35}Cl/^{37}Cl$).

4.14. *N*-4′-Methylphenyl-*Z*-3-chloro-2-(*n*-butylsulfinyl)-propenamide 2m

This was prepared following the procedure described for sulfoxide **2a** using *N*-4′-methylphenyl-*Z*-3-chloro-2-(*n*-butylthio) propenamide **1m** (1.00 g, 3.53 mmol) in acetone (80 mL) and Oxone® (4.34 g, 7.06 mmol) in water (22 mL) for 2 h to give the crude sulfoxide **2m** (1.04 g, 98%). Purification by chromatography on silica gel using ethyl acetate/hexane (10:90) as eluent gave *N*-4′-methylphenyl-*Z*-3-chloro-2-(*n*-butylsulfinyl)-propenamide **2m** (0.95 g, 91%) as a clear oil, which solidified on standing; mp 67–69 °C; $C_{14}H_{18}NClO_2S$ requires C, 56.08; H, 6.05; N, 4.67; Cl, 11.82; S, 10.69. Found: C, 56.39; H, 6.29; N, 4.50; Cl, 11.39; S, 10.24. ν_{max}/cm^{-1} (KBr) 3309 (br NH), 1671 (CO), 1611, 1016 (SO), 819; δ_H 0.96 (3H, t, *J* 7, –CH_3-4′), 1.38–1.63 (2H, m, -CH_2-3′), 1.64-1.91 (2H, m, –CH_2-2′), 2.32 (3H, s, Ar CH_3), 2.88–3.06 (1H, m, one of SOCH_2), 3.09–3.37 (1H, m, one of SOCH_2), 7.14 (2H, d, *J* 8, ArH), 7.49 (2H, d, *J* 8, ArH), 7.78 (1H, s, CHCl=), 10.58 (1H, br s, NH); δ_C 13.43 (CH_3, CH_3-4′), 20.80 (CH_3, CH_3 Ar), 21.70 (CH_2, CH_2-3′), 24.50 (CH_2, CH_2-2′), 52.93 (CH_2, CH_2SO), 120.71, (CH, aromatic CH), 129.81 (CH, aromatic CH), 134.58 (*C*, quaternary aromatic C or SC=), 134.78 (*C*, quaternary aromatic C or SC=), 136.12 (CH, CHCl=), 136.50 (*C*, quaternary aromatic C or SC=), 158.48 (CO); MS *m*/*z* 299 (M^+, 78%), 264 (2, M^+–Cl), 243 (33), 207 (52, M^+–Cl–^{n}Bu), 194 (23, M^+–SO^{n}Bu), 107 (100), 91 (48), 41 (56); isotopic Cl pattern observed; 299, 301 (3:1 ratio $^{35}Cl/^{37}Cl$); Found (HRMS, EI) *m*/*z* 299.0736. $C_{14}H_{18}N^{35}ClO_2S$ requires 299.0747.

4.15. *N*-Phenyl-*Z*-3-chloro-2-(butylsulfinyl)propenamide 2n

This was prepared following the procedure described for sulfoxide **2a** using *N*-phenyl-*Z*-3-chloro-2-(butylthio)propenamide **1n** (2.04 g, 7.1 mmol) in acetone (100 mL) and Oxone® (8.77 g, 14.3 mmol) in water (50 mL) for 2 h to give the sulfoxide **2n**. Following purification by column chromatography on silica gel using hexane/ethyl acetate 95:5 as eluent, the pure sulfoxide **2n** (1.55 g, 76%) was isolated as a clear oil; ν_{max}/cm^{-1} (film) 3524 (NH), 3032 (CH), 1680 (CO), 1568 (NH bend), 1495, 1400 (CN stretch), 1019 (SO); δ_H (300 MHz) 0.97 [3H, t, *J* 7.4, C(4′)H_3], 1.41–1.57 [2H, m, C(3′)H_2], 1.69–1.92 [2H, m, C(2′)H_2], 2.90–3.06 (1H, m, one of SCH_2), 3.13–3.27 (1H, m, one of SCH_2), 7.09–7.19 (1H, m, ArH), 7.21–7.42 (2H, m, ArH), 7.55–7.68 (2H, m, ArH), 7.80 [1H, s, C(3)HCl=], 10.66 (1H, br s, NH); δ_C (75.5 MHz) 13.6 [CH_3, C(4′)H_3], 21.8 [CH_2, C(3′)H_2], 24.6 [CH_2, C(2′)H_2], 52.9 (CH_2, CH_2S), 120.8, 125.0, 129.1 (3 × CH, aromatic CH), 136.2 [C, C(2)S or aromatic *C*], 136.7 [CH, C(3)HCl=], 137.3 [C, C(2)S or aromatic *C*], 158.8 (C, CO); HRMS (ESI): Exact mass calcd for $C_{13}H_{17}NO_2SCl$ $[M+H]^+$, 286.0669. Found 286.0656; 286 ($[M+H]^+$, 100%).

4.16. *N*-4′-Methylphenyl-*Z*-3-chloro-2-(4′-methoxybenzenesulfinyl)propenamide 2o

This was prepared using the procedure described for sulfoxide **2a** using *N*-4′-methylphenyl-*Z*-3-chloro-2-(4′-methoxybenzenethio)propenamide **1o** (0.70 g, 2.10 mmol) in acetone (70 mL) and Oxone® (3.88 g, 6.30 mmol) in water (30 mL) overnight to give the crude sulfoxide **2o** (0.71 g, 96%) as a colourless solid. Further purification was not required although previously samples have been purified by chromatography on silica gel using ethyl acetate/hexane (70:30) as eluent (84%) or trituration from ether (80%); mp 128–130 °C; $C_{17}H_{16}NClO_3S$ requires C, 58.36; H, 4.61; N, 4.00; Cl, 10.13; S, 9.16. Found: C, 58.16; H, 4.62; N, 4.07; Cl, 10.27; S, 9.62 (extra combustion required for S analysis). ν_{max}/cm^{-1} (KBr) 3050 (NH), 1670 (CO), 1612, 1495, 1260, 1023, 725; δ_H 2.31 (3H, s, Ar CH_3), 3.81 (3H, s, OCH_3), 6.99 (2H, half of ABq, *J* 9, ArH), 7.13 (2H, half of ABq, *J* 8, ArH), 7.47 (2H, half of ABq, *J* 8, ArH), 7.63 (2H, half of ABq, *J* 9, ArH), 7.75 (1H, s, CHCl=), 10.53 (1H, br s, NH); δ_C 20.92 (Ar CH_3), 55.58 (OCH_3), 115.37 (aromatic CH), 120.71 (aromatic CH), 126.32 (aromatic CH), 129.58 (aromatic CH), 131.82 (quaternary aromatic C or SC=), 134.64 (quaternary aromatic C or SC=), 134.79 (quaternary aromatic C or SC=), 136.80 (CHCl=), 138.40 (quaternary aromatic C or SC=), 158.39 (*C*-OMe), 162.69 (CO); MS *m*/*z* 349 (M^+, 40%), 213 (40), 155 (100, $[SOAr]^+$), 106 (50), 77 (50); isotopic Cl pattern observed; 349, 351 (3:1 ratio $^{35}Cl/^{37}Cl$); Found (HRMS, EI) *m*/*z* 349.0536. $C_{17}H_{16}N^{35}ClO_3S$ requires 349.0540.

4.17. *N*-Benzyl-*Z*-3-chloro-2-(4′-methoxybenzenesulfinyl)propenamide 2p

This was prepared using the procedure described for sulfoxide **2p** using *N*-benzyl-*Z*-3-chloro-2-(4′-methoxybenzene-thio)propenamide **1p** (330 mg, 0.99 mmol) in acetone (10 mL) and Oxone® (1.80 g, 2.97 mmol) in water (9 mL) overnight to give the crude sulfoxide **2p** (320 mg, 93%) as a clear oil. Further purification was not conducted; ν_{max}/cm^{-1} (film) 3280 (NH), 1660 (CO), 1593, 1495, 1085, 1027, 830; δ_H 3.83 (3H, s, OCH_3), 4.28–4.79 (2H, m, NCH_2), 6.88–6.97 (2H, m, ArH), 7.11–7.36 (5H, m, ArH), 7.45–7.53 (2H, m, ArH), 7.72 (1H, s, CHCl=), 8.86 (1H, br s, NH); MS *m*/*z* 349 (M^+, 18%), 333 (3, M^+–O), 155 (94, $[SOAr]^+$), 139 (22), 91

(100); isotopic Cl pattern observed; 349, 351 (3:1 $^{35}Cl/^{37}Cl$); Found (HRMS, EI) m/z 349.0523. $C_{17}H_{16}N^{35}ClO_3S$ requires 349.0540.

4.18. *N*-Ethyl-*Z*-3-chloro-2-(4′-methoxybenzenesulfinyl)propenamide 2q

This was prepared using the procedure described for sulfoxide **2a** using *N*-ethyl-*Z*-3-chloro-2-(4′-methoxybenzene-thio)propenamide **1q** (0.50 g, 1.84 mmol) in acetone (40 mL) and Oxone® (2.27 g, 3.68 mmol) in water (11 mL) for 1 h to give **2q** as a yellow oil (0.53 g, 100%). The crude product was purified by chromatography on silica gel using ethyl acetate/hexane (20:80) as eluent to give the sulfoxide **2q** (0.51 g, 96%) as a colourless solid; mp 53.5–55 °C; $C_{12}H_{14}NClO_3S$ requires C, 50.08; H, 4.90; N, 4.87; Cl, 12.32; S, 11.14. Found: C, 50.20; H, 5.00; N, 4.54; Cl, 12.34; S, 11.48. ν_{max}/cm^{-1} (KBr) 1662 (CO), 1570, 1496, 1259, 1023, 837; δ_H 1.16 (3H, t, *J* 7, $-CH_3$), 3.19–3.43 (2H, m, NCH_2), 3.87 (3H, s, OCH_3), 7.01–7.62 (4H, ABq, *J* 5, ArH), 7.71 (1H, s, CHCl=), 8.47 (1H, br s, NH); δ_C 14.92 ($-CH_3$), 34.72 (NCH_2), 56.02 (OCH_3), 115.65 (aromatic CH), 126.75 (aromatic CH), 132.72 (quaternary aromatic or SC=), 136.41 (CHCl=), 139.60 (quaternary aromatic or SC=), 160.94 (C-OMe), 163.05 (CO); MS m/z 287 (M^+, 7%), 271 (3, M^+-O), 199 (35, $M^+-CONHEt-O$), 155 (48, $[SOAr]^+$), 72 (100); isotopic Cl pattern observed; 287, 289 (3:1 ratio $^{35}Cl/^{37}Cl$); Found (HRMS, EI) m/z 287.0383. $C_{12}H_{14}N^{35}ClO_3S$ requires 287.0383.

4.19. *N*-4′-Methylphenyl-*Z*-3-chloro-2-(4-nitrobenzenesulfinyl)propenamide 2r

This was prepared using the procedure described for sulfoxide **2a** using *N*-4′-methylphenyl-*Z*-3-chloro-2-(4-nitrobenzenesulfinyl)propenamide **1r** (0.44 g, 1.26 mmol) in acetone (35 mL) and Oxone® (1.55, 2.53 mmol) in water (8 mL). However, after 2 h, TLC showed substantial starting material remaining. A further TLC was run after 6 h and this again showed starting material remaining. The reaction mixture was stirred for 28 h before work-up to give **2r** as a yellow oil. The crude product was purified by chromatography on silica gel using ethyl acetate/hexane (30:70) as eluent to give the sulfoxide **2r** (0.39 g, 84%) as a yellow solid; mp 151–153 °C; $C_{16}H_{13}N_2ClO_4S$ requires C, 52.68; H, 3.59; N, 7.68; Cl, 9.72; S, 8.79. Found: C, 53.00; H, 3.80; N, 7.52; Cl, 10.13; S, 8.98. ν_{max}/cm^{-1} (KBr) 1673 (CO), 1523, 1346, 1036 (SO), 854; δ_H 2.32 (3H, s, Ar CH_3), 7.14 (2H, d, *J* 11, ArH), 7.38 (2H, d, *J* 11, ArH), 7.88–7.96 (3H, m, ArH, CHCl=), 8.39 (2H, d, *J* 16, ArH), 10.02 (1H, br s, NH); δ_C 20.89 (Ar CH_3), 120.67 (aromatic CH), 124.89 (aromatic CH), 125.33 (aromatic CH), 129.71 (aromatic CH), 134.33 (quaternary aromatic), 135.17 (quaternary aromatic), 138.38 (quaternary aromatic), 138.95 (CHCl=), 148.17, 150.10 (quaternary aromatic and SC=), 157.52 (CO); MS m/z 364 (M^+, 20), 348 (1, M^+-O), 228 (16), 170 (23, $[SOAr]^+$), 106 (50, $[NHTol]^+$), 77 (78), 43 (100); isotopic Cl pattern observed; 364, 366 (3:1 $^{35}Cl/^{37}Cl$); Found (HRMS, EI) 364.0281. $C_{16}H_{13}N_2{}^{35}ClO_4S$ requires 364.0285.

4.20. *N*-4′-Fluorophenyl-*Z*-3-chloro-2-(*iso*-butylsulfinyl)propenamide 2s

This was prepared using the procedure described for sulfoxide **2a** using Oxone® (4.71 g, 7.66 mmol) in water (5 mL) and **1s** (1.10 g, 3.83 mmol) in acetone (66 mL) at room temperature. The crude product was purified by chromatography on silica gel using ethyl acetate/hexane (20:80) as eluent to give the sulfoxide **2s** (1.14 g, 92%) as a yellow oil, which solidified on standing; mp 65–67 °C; $C_{13}H_{15}NClO_2SF$ requires C, 51.40; H, 4.98; N, 4.61; Cl, 11.67; S, 10.56. Found: C, 51.15; H, 5.00; N, 4.61; Cl, 11.76, F, 6.00; S, 10.90. ν_{max}/cm^{-1} (KBr) 3294 (br, NH), 1680 (CO), 1540, 1082, δ_H 1.14 [3H, d, *J* 6.7 one of $CH(CH_3)_2$], 1.17 [3H, d, *J* 6.7 one of $CH(CH_3)_2$], 2.13–2.39 [1H, m, H_X of ABX system, $CH(CH_3)_2$], 2.61–2.79 (1H, m, H_A of ABX system, SCH_A), 3.10–3.23 (1H, m, H_B of ABX system, SCH_B), 6.98–7.06 (2H, m, Ar-3′-H), 7.49–7.58 (2H, m, Ar-2′-H), 7.76 (1H, s, CHCl=), 10.70 (1H, br s, NH); δ_C 21.37 [CH_3, one of $CH(CH_3)_2$], 22.69 [CH_3, one of $CH(CH_3)_2$], 24.21 [CH, $CH(CH_3)_2$], 62.44 (CH_2, $SOCH_2$), 115.76 (CH, d, $^3J_{CF}$ 22.6, aromatic CH, ArC-3′), 122.43 (CH, d, *J* 7.9, aromatic CH, ArC-2′), 133.38 (C, quaternary aromatic or SC=), 136.24 (2×CH, quaternary aromatic, CHCl=), 158.05/161.29 (C, d, $^4J_{CF}$ 244.6, quaternary aromatic, ArC-4′), 158.65 (CO); MS m/z M^+(303,15), $M^+-Cl-{}^iBu$ (211, 12), 111(55), 57 (100); isotopic Cl pattern observed; 303:305 (3:1 ratio $^{35}Cl/^{37}Cl$): Found (HRMS, EI) m/z 303.04961 $C_{13}H_{15}SNO_2{}^{35}ClF$ requires 303.04958.

4.21. *N*-4′-Fluorophenyl-*Z*-3-chloro-2-(*iso*-propylsulfinyl)propenamide 2t

This was prepared using the procedure described for sulfoxide **2a** using *N*-4′-fluorophenyl-*Z*-3-chloro-2-(methylthio)propenamide **1t** (1 g, 3.65 mmol), Oxone® (4.5 g, 7.31 mmol), acetone (60 mL) and water (25 mL). Purification by chromatography on silica gel using ethyl acetate/hexane (80:20) as eluent gave the sulfoxide **2t** (0.97 g, 88%) as a white solid; mp 78–80 °C; $C_{12}H_{13}SNO_2ClF$ requires C, 49.74; H, 4.52; N, 4.83; S, 11.07. Found: C, 49.75; H, 4.48; N, 4.61; S, 11.40. ν_{max}/cm^{-1} (KBr) 3326, 1672, 1509, 1212, 832; δ_H 1.31–1.59 [6H, m, $CH(CH_3)_2$], 3.19–3.39 [1H, m, $CH(CH_3)_2$], 7.03–7.09 (2H, m, ArH-3), 7.45 (2H, m, ArH-2), 7.80 (1H, s, =CHCl), 10.90 (1H, br s, NH); δ_C 15.29 [CH_3, $CH(CH_3)_2$], 16.35 [CH_3, $CH(CH_3)_2$], 53.55 [CH, $CH(CH_3)_2$], 115.74 (CH, d, $^2J_{CF}$ 22.57, aromatic CH, ArC-3), 122.33 (CH, d, $^3J_{CF}$ 7.92, aromatic CH, ArC-2), 133.37 (C, =SC), 134.86 (C, d, $^4J_{CF}$ 2.88, quaternary aromatic C, ArC-1), 138.11 (CH, =CHCl), 158.00/161.24 (C, d, $^1J_{CF}$ 248.02, quaternary aromatic C, ArC-4), 159.28 (CO); MS m/z 289 (M^+, 10%), 247 (100%), 239 (40%), 222 (30%).

4.22. *N*-4′-Fluorophenyl-*Z*-3-chloro-2-(methylsulfinyl)propenamide 2u

This was prepared using the procedure described for sulfoxide **1a** using *N*-4′-fluorophenyl-*Z*-3-chloro-2-(methylthio)propenamide (1.00 g, 4.07 mmol) **2u** and Oxone® (5.00 g, 8.15 mmol), acetone (60 mL) and water (25 mL) Purification by chromatography on silica gel using ethyl acetate/hexane (80:20) as eluent gave the sulfoxide **2u** (0.98 g, 92%) as a white solid; mp 97–99 °C; $C_{10}H_9SNO_2ClF$ requires C, 45.89; H, 3.47; N, 5.35; S, 12.25. Found: C, 45.91; H, 3.44; N, 5.23; S, 12.49. ν_{max}/cm^{-1} (KBr) 1670, 1509, 1211; δ_H 2.94 (3H, s, SCH_3), 6.98–7.07 (2H, m, ArH-3), 7.59–7.67 (2H, m, ArH-2), 7.76 (1H, s, =CHCl), 10.67 (1H, br s, NH); δ_C 39.53 (CH_3, SCH_3), 116.11 (CH, d, $^2J_{CF}$ 22.49, aromatic CH, ArC-3), 122.79 (CH, d, $^3J_{CF}$ 7.92, aromatic CH, ArC-2), 132.72 (C, d, $^4J_{CF}$ 2.57, quaternary aromatic C, ArC-1), 136.66 (CH, =CHCl), 139.09 (C, =SC), 158.36/161.60 (C, d, $^1J_{CF}$ 244.52, quaternary aromatic C, ArC-4), 158.61 (CO); MS m/z 261, (M^+, 20%), 198 (9%), 164 (10%), 151 (30); isotopic Cl pattern observed; 261:263 (3:1 ratio $^{35}Cl/^{37}Cl$).

4.23. *N*-*n*-Butyl-*Z*-3-chloro-2-(methylsulfinyl)propenamide 2v

This was prepared using the procedure described for sulfoxide **2a** using *N*-*n*-butyl-*Z*-3-chloro-2-(methylthio)propenamide **1v** (1.24 g, 5.98 mmol), Oxone® (7.35 g, 11.96 mmol) in acetone (74 mL) and water (40 mL). Purification by chromatography on silica gel using ethyl acetate/hexane (80:20) as eluent gave the sulfoxide **2v** (1.14g, 85%) as a colourless oil; $C_8H_{14}SNO_2Cl$ requires C, 43.95; H, 6.31; N, 6.26; S, 14.33. Found: C, 42.62; H, 6.27; N,

6.18; S, 14.02. ν_{max}/cm^{-1} (film) 3278, 1665, 1572; δ_H 0.94 (3H, t, *J* 7.3, C*H*$_3$-4′), 1.31–1.51 (2H, m, C*H*$_2$-3′), 1.52–1.69 (2H, m, C*H*$_2$-2′), 2.85 (3H, s, SCH$_3$), 3.35 (2H, q, *J* 6.0, NCH$_2$), 7.71 (1H, s, =CHCl), 8.59 (1H, br s, NH); δ_C 13.71 (CH$_3$, *C*H$_3$-4′), 20.20 (CH$_3$, SCH$_3$), 31.26 (CH$_2$, *C*H$_2$-3′), 38.99 (CH$_2$, *C*H$_2$-2′), 39.27 (CH$_2$, NCH$_2$), 135.08 (C, S*C*=), 137.65 (CH, =*C*HCl), 160.48 (CO); MS *m*/*z* 223 (M$^+$, 1%), 222 (10%), 205 (100%).

4.24. *N*-Benzyl-*Z*-3-chloro-2-(methylsulfinyl)propenamide 2w

This was prepared using the procedure described for sulfoxide **2a** using *N*-benzyl-*Z*-3-chloro-2-(methylthio)propenamide **1w** (0.35 g, 1.69 mmol), Oxone® (2.07 g, 1.69 mmol) in acetone (21 mL) and water (11 mL). Purification by chromatography on silica gel using ethyl acetate/hexane (80:20) as eluent gave the sulfoxide **2w** (0.31 g, 82%) as a colourless oil; $C_{11}H_{12}SNO_2Cl$ requires C, 51.36; H, 4.66; N, 5.44; S, 12.45. Found: C, 51.32; H, 4.60; N, 5.31; S, 12.15. ν_{max}/cm^{-1} (film) 3290, 1644, 1519; δ_H 2.86 (3H, s, SC*H*$_3$), 4.42–4.68 (2H, m, CH$_2$Ph), 7.12–7.41 (5H, m, ArH), 7.71 (1H, s, =C*H*Cl); 8.99 (1H, br s, NH); δ_C 38.93 (CH$_3$, SCH$_3$), 43.98 (CH$_2$, CH$_2$Ph), 127.50 (2 × CH, ArCH), 127.60 (2 × CH, ArCH), 128.72 (C, =*S*C), 135.55 (CH, =*C*HCl), 137.51 (C, quaternary aromatic C), 160.59 (CO); MS *m*/*z* No M$^+$, 240 (30%), 158 (45%), 135 (32%).

4.25. *N*-Benzyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide 2x

This was prepared using the procedure described for sulfoxide **2a** using a solution of Oxone® (7.74 g, 12.6 mmol) in water (40 mL) and *N*-4′-benzyl-*Z*-3-chloro-2-(benzylthio)propenamide **1x** (2.00 g, 6.3 mmol) in acetone (150 mL) at room temperature. Following purification by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 2–10% ethyl acetate), **2x** (1.44 g, 69%) was isolated as a clear oil; ν_{max}/cm^{-1} (film) 3258 (NH), 3061 (CH), 1661 (CO), 1572 (NH bend), 1496, 1454 (CN stretch), 1023 (SO); δ_H (300 MHz, $CDCl_3$) 4.23 (1H, A of ABq, *J* 12.8, one of SC*H*$_2$), 4.31 (1H, B of ABq, *J* 12.8, one of SC*H*$_2$), 4.27–4.33 (1H, A of ABX, J_{AB} 14.9, J_{AX} 5.6, C*H*$_2$NH), 4.45–4.52 (1H, B of ABX, J_{AB} 14.9, J_{BX} 5.6, C*H*$_2$NH), 7.18–7.38 (10H, m, Ar*H*), 7.79 [1H, s, C(3)*H*Cl=], 8.63 (1H, br s, N*H*); δ_C (75.5, $CDCl_3$) 43.8 (CH$_2$, *C*H$_2$NH), 58.8 (CH$_2$, SCH$_2$), 127.9, 128.1, 129.1, 129.2, 129.4, 131.0 (CH, aromatic *C*H), 135.8 [C, aromatic *C* or *C*(2)S], 137.0 [CH, *C*(3)HCl=], 137.8 [C, aromatic *C* or *C*(2)S], 161.1 (C, *C*O); HRMS (ESI): Exact mass calcd for $C_{17}H_{16}NO_2SClNa$ [M+Na]$^+$, 356.0488. Found 356.0490; 334 ([M+H]$^+$, 100%), 91 ($C_7H_7^+$, 70%); isotopic Cl pattern observed; 334, 336 (3:1 $^{35}Cl/^{37}Cl$).

4.26. *N*-4′-Fluorophenyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide 2y

The title compound was synthesised following the procedure outlined for **2a** using *N*-4′-fluorophenyl-*Z*-3-chloro-2-(benzylthio)propenamide **1y** (1.05 g, 3.3 mmol) in acetone (80 mL) and Oxone® (4.00 g, 6.5 mmol) in water (15 mL). Following stirring at room temperature for 2 h, the crude **2y** was obtained as an off-white solid. This was then purified by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 2–5% ethyl acetate) to give the pure product (0.84 g, 77%) as a white solid, mp 121–122 °C; ($C_{16}H_{13}NClFO_2S$ requires C, 56.89; H, 3.88; N, 4.15; S, 9.49; Cl, 10.50; F, 5.62. Found: C, 56.76; H, 3.81; N, 4.05; S, 9.67; Cl, 10.68; F, 5.89.); ν_{max}/cm^{-1} (KBr) 3201 (NH), 3060 (CH), 1670 (CO), 1573 (NH bend), 1508, 1409 (CN stretch), 1025 (SO); δ_H (300 MHz, $CDCl_3$) 4.27 (2H, s, SC*H*$_2$), 6.96 [2H, overlapping dd (appears as a triplet), *J* 8.6, 8.6, C(3′)*H*], 7.19–7.40 (8H, m, Ar*H*), 7.81 [1H, s, C(3)*H*Cl=], 10.08 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 58.7 (CH$_2$, SCH$_2$), 115.9 [CH, d, $^2J_{CF}$ 22, aromatic *C*H, ArC(3′)], 122.6 [CH, d, $^3J_{CF}$ 8, aromatic *C*H, ArC(2′)], 129.3, 129.6, 131.0 (CH, aromatic *C*H), 133.1, 134.8 [C, aromatic *C* or *C*(2)S], 137.5 [CH, *C*(3)HCl=], 159.6 [*C*, d, $^1J_{CF}$ 245, aromatic *C*, ArC(4′)], 158.4 (C, *C*O); *m*/*z* (ESI) 360 ([M+Na]$^+$, 6%), 91 ($C_7H_7^+$, 100%).

4.27. *N*-*n*-Butyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide 2z

This was prepared following the procedure described for **2a** using *N*-*n*-butyl-*Z*-3-chloro-2-(benzylthio)propenamide **1z** (0.32 g, 1.1 mmol) in acetone (20 mL) and Oxone® (1.39 g, 2.3 mmol) in water (10 mL) for 2 h to give **2z**. Following purification by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 2–10% ethyl acetate), **2z** (0.23 g, 69%) was isolated as a clear oil; ν_{max}/cm^{-1} (film) 3400 (NH), 1646 (CO), 1560 (NH bend), 1457, 1402 (CN stretch), 1045 (SO); δ_H (300 MHz, $CDCl_3$) 0.91 [3H, t, *J* 7.1, C(4′)*H*$_3$], 1.23–1.46 [4H, m, C(3′)*H*$_2$ and C(2′)*H*$_2$], 2.99–3.27 (2H, m, C*H*$_2$NH), 4.19 (1H, A of ABq, *J* 12.8, one of SC*H*$_2$), 4.25 (1H, B of ABq, *J* 12.8, one of SC*H*$_2$), 7.23–7.41 (5H, m, Ar*H*), 7.61 [1H, s, C(3)*H*Cl=], 8.19 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 14.1 [CH$_3$, *C*(4′)H$_3$], 20.6 [CH$_2$, *C*(3′)H$_2$], 31.5 [CH$_2$, *C*(2′)H$_2$], 39.5 (CH$_2$, *C*H$_2$N), 58.8 (CH$_2$, SCH$_2$), 128.6 (C, aromatic *C*), 129.2, 129.4, 131.0 (3 × CH, aromatic *C*H), 135.8, [C, *C*(2)S], 136.4 [C, *C*(3)HCl=], 161.0 (C, *C*O); HRMS (ESI): Exact mass calcd for $C_{14}H_{19}NO_2SCl$ [M+H]$^+$, 300.0825. Found 300.0826; 322 ([M+Na])$^+$, 8%, 91 ($C_7H_7^+$, 100%).

4.28. *N*-4′-Methylphenyl-*Z*-3-chloro-2-(benzylsulfinyl)-propenamide 2aa

This was synthesised according to the procedure outlined for **2a** using *N*-4′-methylphenyl-*Z*-3-chloro-2-(benzylthio)propenamide **1aa** (0.50 g, 1.6 mmol) in acetone (50 mL) and Oxone® (1.93 g, 3.2 mmol) in water (15 mL). The reaction mixture was stirred at room temperature for 2 h and following the work-up, **2aa** was obtained as an off-white solid. This was then purified by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 2–5% ethyl acetate) to give **2aa** (0.38 g, 72%) as a white solid, mp 116–118 °C; ($C_{17}H_{16}ClNO_2S$ requires C, 61.61; H, 4.83; N, 4.20; S, 9.61; Cl, 10.62. Found: C, 61.05; H, 4.62; N, 4.32; S, 9.48; Cl, 10.63.); ν_{max}/cm^{-1} (KBr) 3056 (NH), 1673 (CO), 1560 (NH bend), 1513, 1408 (CN stretch), 1023 (SO); δ_H (300 MHz, $CDCl_3$) 2.36 (3H, s, Ar-C*H*$_3$), 4.25 (1H, A of ABq, *J* 13.0, one of SC*H*$_2$), 4.30 (1H, B of ABq, *J* 13.0, one of SC*H*$_2$), 7.00–7.41 (9H, m, Ar*H*), 7.79 [1H, s, C(3)*H*Cl=], 10.10 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 21.4 (CH$_3$, Ar-*C*H$_3$), 58.9 (CH$_2$, SCH$_2$), 121.1 (CH, aromatic *C*H), 128.2 [C, aromatic *C* or *C*(2)S], 129.3, 129.5, 129.7, 131.0 (CH, aromatic *C*H), 134.9, 135.0, 135.6 [C, aromatic *C* or *C*(2)S], 137.3 [CH, *C*(3)HCl=], 158.6 (C, *C*O); *m*/*z* (ESI) 334 ([M+H]$^+$, 100%), 91 ($C_7H_7^+$, 48%); isotopic Cl pattern observed; 334, 336 (3:1 $^{35}Cl/^{37}Cl$).

4.29. *N*-Methyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide 2ab

The title compound was synthesised following the procedure outlined for **2a** using *N*-methyl-*Z*-3-chloro-2-(benzylthio)propenamide **1ab** (2.00 g, 8.0 mmol) in acetone (150 mL) and Oxone® (10.14 g, 16.5 mmol) in water (40 mL). The crude sulfoxide was obtained as a pale yellow oil and following purification by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 20–40% ethyl acetate), **2ab** (1.36 g, 66%) was isolated as a clear oil; ν_{max}/cm^{-1} (film) 3240 (NH), 3061 (CH), 1667 (CO), 1567 (NH bend), 1496, 1411 (CN stretch), 1030 (SO); δ_H (300 MHz, $CDCl_3$) 2.65 (3H, d, *J* 4.8, C*H*$_3$NH), 4.21 (2H, s, SC*H*$_2$), 7.19–7.37 (5H, m, Ar*H*), 7.70 [1H, s, C(3)*H*Cl=], 8.06 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 25.9 (CH$_3$, *C*H$_3$NH), 58.4 (CH$_2$, SCH$_2$), 128.1 [C, aromatic *C* or *C*(2)S], 128.8, 129.0, 130.7 (CH, aromatic *C*H), 135.4 [C, aromatic *C* or *C*(2)S], 136.1 [CH, *C*(3)HCl=], 161.3

(C, *C*O); Exact mass calcd for $C_{11}H_{12}NO_2SClNa$ $[M+Na]^+$, 280.0175. Found 280.0175; 258 ($[M+H]^+$, 80%), 91 ($C_7H_7^+$, 100%); isotopic Cl pattern observed; 258, 260 (3:1 $^{35}Cl/^{37}Cl$).

4.30. *N*-Phenyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide 2ac

This was prepared following the procedure described for **2a** using *N*-phenyl-*Z*-3-chloro-2-(benzylthio)propenamide **1ac** (1.49 g, 4.9 mmol) in acetone (120 mL) and Oxone® (6.04 g, 9.8 mmol) in water (30 mL). The crude sulfoxide **2ac** (1.19 g, 76%) was isolated as a white solid, which was carried forward without further purification, mp 105–107 °C; ($C_{16}H_{14}NO_2SCl$ requires C, 60.09; H,4.41; Cl, 11.09; S, 10.03. Found: C, 59.49; H, 4.30; Cl, 11.16; N, 4.39; S, 9.99.); ν_{max}/cm^{-1} (KBr) 3435 (NH), 3061 (CH), 1672 (CO), 1609, 1564 (NH bend), 1494, 1409 (CN stretch), 1024 (SO); δ_H (300 MHz, $CDCl_3$) 4.29 (2H, s, S*CH*$_2$), 7.04–7.50 (10H, m, Ar*H*), 7.81 [1H, s, C(3)*H*Cl=], 10.08 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 58.5 (CH_2, S*CH*$_2$), 120.7, 124.8 (CH, aromatic *C*H), 127.7 [C, *C*(2)S or aromatic *C*], 128.8, 128.9, 129.1, 130.5 (CH, aromatic *C*H), 135.1, 137.1 [C, *C*(2)S or aromatic *C*], 137.2 [CH, *C*(3)HCl=], 158.4 (C, *C*O); Exact mass calcd for $C_{16}H_{14}NO_2SClNa$ $[M+Na]^+$, 342.0331. Found 342.0331; 320 ($[M+H]^+$, 100%), 91 ($C_7H_7^+$, 66%); isotopic Cl pattern observed; 320, 322 (3:1 $^{35}Cl/^{37}Cl$).

4.31. *Z*-3-Chloro-2-(benzylsulfinyl)propenamide 2ad

The title compound was synthesised according to the procedure outlined for **2a** using *Z*-3-chloro-2-(benzylthio)propenamide **1ad** (0.24 g, 1.1 mmol) in acetone (20 mL) and Oxone® (1.29 g, 2.1 mmol) in water (5 mL), to give the crude sulfoxide as an off-white solid. Following purification by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 5–40% ethyl acetate), the pure sulfoxide **2ad** (0.12 g, 46%) was isolated as a white solid, mp 115–117 °C; ($C_{10}H_{10}NO_2SCl$ requires C, 49.28; H, 4.14; Cl, 14.55; N, 5.75; S, 13.16. Found: C, 49.33; H, 4.15; Cl, 14.99; N, 5.75; S, 12.94.); ν_{max}/cm^{-1} (KBr) 3433 (NH), 1646 (CO), 1026 (SO); δ_H (300 MHz, $CDCl_3$) 4.22 (1H, A of ABq, *J* 12.8, one of S*CH*$_2$), 4.31 (1H, B of ABq, *J* 12.8, one of S*CH*$_2$), 5.65 (1H, br s, one of N*H*$_2$), 7.17–7.48 (5H, m, Ar*H*), 7.73 [1H, s, C(3)*H*Cl=], 8.19 (1H, br s, one of N*H*$_2$); δ_C (75.5 MHz, $CDCl_3$) 58.6 (CH_2, S*CH*$_2$), 128.1 [C, aromatic *C* or *C*(2)S], 128.9, 129.0, 130.6 (CH, aromatic *C*H), 135.8 [C, aromatic *C* or *C*(2)S], 137.9 [CH, *C*(3)HCl=], 161.8 (C, *C*O); m/z (ESI) 244 ($[M+H]^+$, 100%), 91 ($C_7H_7^+$, 62%); isotopic Cl pattern observed; 244, 246 (3:1 $^{35}Cl/^{37}Cl$).

4.32. *N*,*N*-Dimethyl-*E*-3-chloro-2-(benzylsulfinyl)propenamide 2ae

The title compound was prepared following the procedure described for **2a** using *N*,*N*-dimethyl-*E*-3-chloro-2-(benzylthio)-propenamide **1ae** (1.00 g, 3.9 mmol) in acetone (100 mL) and Oxone® (4.81 g, 7.8 mmol) in water (30 mL) for 2 h to give the crude sulfoxide **2ae** as a white solid. Following purification by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 0–20% ethyl acetate), the pure sulfoxide **2ae** (0.80 g, 75%) was isolated as a white solid, mp 111–113 °C; ν_{max}/cm^{-1} (KBr) 3069 (CH stretch), 1643 (CO), 1495, 1403 (CN stretch), 1078 (SO); δ_H (300 MHz, $CDCl_3$) 3.10 [3H, s, one of N(C*H*$_3$)$_2$], 3.13 [3H, s, one of N(C*H*$_3$)$_2$], 4.36 (1H, A of ABq, *J* 13.9, one of SOC*H*$_2$), 4.74 (1H, B of ABq, *J* 13.9, one of SOC*H*$_2$), 6.82 [1H, s, C(3)*H*Cl=], 7.35–7.42 (3H, m, Ar*H*), 7.47–7.55 (2H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 35.3 [CH_3, one of N(*C*H$_3$)$_2$], 37.9 [CH_3, one of N(*C*H$_3$)$_2$], 61.4 (CH_2, S*CH*$_2$), 127.9 [C, aromatic *C* or *C*(2)S], 129.1, 129.5, 131.8 (CH, aromatic *C*H), 135.2 [CH, *C*(3)HCl=], 137.2 [C, aromatic *C* or *C*(2)S], 161.4 (C, *C*O).

4.33. *N*,*N*-Dimethyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide 2af

The title compound was prepared following the procedure described for **2a** using *N*,*N*-dimethyl-*Z*-3-chloro-2-(benzylthio)propenamide **1af** (1.00 g, 3.9 mmol) in acetone (100 mL) and Oxone® (4.81 g, 7.8 mmol) in water (30 mL) for 2 h to give the crude sulfoxide **2af** as a yellow oil. Following purification by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 0–20% ethyl acetate), the pure sulfoxide **2af** (0.80 g, 75%) was isolated as a yellow oil; ν_{max}/cm^{-1} (film) 3032 (CH), 1645 (CO), 1496, 1052 (SO); δ_H (300 MHz, $CDCl_3$) 3.10 [6H, d, *J* 1.7, N(C*H*$_3$)$_2$], 4.46 (1H, A of ABq, *J* 12.2, one of SOC*H*$_2$), 4.58 (1H, B of ABq, *J* 12.2, one of SOC*H*$_2$), 6.59 [1H, s, C(3)*H*Cl=], 7.31–7.38 (3H, m, Ar*H*), 7.43–7.51 (2H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 35.2 [CH_3, one of N(*C*H$_3$)$_2$], 39.0 [CH_3, one of N(*C*H$_3$)$_2$], 60.1 (CH_2, S*CH*$_2$), 125.3, 128.5, 128.8 (CH, aromatic *C*H), 129.1 (C, aromatic *C* or *C*(2)S), 130.9 [CH, *C*(3)HCl=], 142.0 [C, aromatic *C* or *C*(2)S], 162.0 (C, *C*O); HRMS (ESI): Exact mass calcd for $C_{12}H_{15}NO_2SCl$ $[M+H]^+$, 272.00512. Found 272.0500; 272 ($[M+H]^+$, 100%); isotopic Cl pattern observed; 272, 274 (3:1 $^{35}Cl/^{37}Cl$).

4.34. *N*-4′-Fluorophenyl-*Z*-3-chloro-2-(benzylsulfinyl)-2-butenamide 2ag

The title compound was synthesised following the procedure outlined for sulfoxide **2a** using *N*-4′-fluorophenyl-*Z*-3-chloro-2-(benzylthio)-2-butenamide **1ag** (1.35 g, 4.0 mmol) in acetone (110 mL) and Oxone® (4.95 g, 8.0 mmol) in water (25 mL). Following stirring at room temperature for 2 h, the crude sulfoxide **2ag** was obtained as a yellow oil. This was then purified by column chromatography on silica gel using hexane/ethyl acetate (98:2) as eluent to give the pure product (1.17 g, 83%) as a white solid, mp 152–153 °C; ($C_{17}H_{15}NClFO_2S$ requires C, 58.04; H, 4.30; N, 3.98; S, 9.11; Cl, 10.08; F, 5.40. Found: C, 57.83; H, 4.26; N, 3.71; S, 9.53; Cl, 10.50; F, 5.40.); ν_{max}/cm^{-1} (KBr) 3251 (NH), 3062 (CH), 1671 (CO), 1612 (NH bend), 1514, 1407 (CN stretch), 1034 (SO); δ_H (300 MHz, $CDCl_3$) 2.59 (3H, s, C*H*$_3$CCl=), 4.18 (1H, A of ABq, J_{AB} 13.4, one of SC*H*$_2$), 4.26 (1H, B of ABq, J_{AB} 13.4, one of SC*H*$_2$), 7.00 [2H, overlapping dd (appears as a triplet), *J* 8.5, 8.5, C(3′)*H*], 7.26–7.59 (7H, m, Ar*H*), 9.86 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 27.2 (CH_3, *C*H$_3$CCl=), 58.7 (CH_2, S*CH*$_2$), 116.0 [CH, d, $^2J_{CF}$ 22, aromatic *C*H, ArC(3′)], 122.5 [CH, d, $^3J_{CF}$ 8, aromatic *C*H, ArC(2′)], 129.2, 129.3, 130.9, (3 × CH, 3 × aromatic *C*H), 128.6, 131.3, 133.9, 152.5 [4 × C, aromatic *C*, *C*(2)S or *C*(3)Cl], 159.7 [*C*, d, $^1J_{CF}$ 245, aromatic *C*, ArC(4′)], 160.4 (C, *C*O); m/z (ESI) 352 ($[M+H]^+$, 100%), 91 ($C_7H_7^+$, 18%).

4.35. *N*-4′-Fluorophenyl-*E*-3-chloro-2-(benzylsulfinyl)-2-butenamide 2ah

The title compound was synthesised following the procedure outlined for sulfoxide **2a** using *N*-4′-fluorophenyl-*E*-3-chloro-2-(benzylthio)-2-butenamide **1ah** (0.42 g, 1.2 mmol) in acetone (40 mL) and Oxone® (1.53 g, 2.5 mmol) in water (10 mL). Following stirring at room temperature for 2 h, the crude sulfoxide **2ah** was obtained as a yellow solid. This was then purified by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 20–40% EtOAc) to give the pure product (0.22 g, 53%) as a colourless oil; ν_{max}/cm^{-1} (NaCl) 3250 (NH), 3068 (CH), 1672 (CO), 1618 (NH bend), 1508, 1408 (CN stretch), 1034 (SO); δ_H (300 MHz, $CDCl_3$) 1.93 (3H, s, C*H*$_3$CCl=), 4.30 (1H, A of ABq, J_{AB} 12.2, one of SC*H*$_2$), 4.41 (1H, B of ABq, J_{AB} 12.2, one of SC*H*$_2$), 7.05 [2H, overlapping dd (appears as a triplet), *J* 9.0, 9.0, C(3′)*H*], 7.34–7.39 (5H, m, Ar*H*), 7.60–7.64 (2H, m, Ar*H*), 8.76 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 23.7 (CH_3, *C*H$_3$CCl=), 58.8 (CH_2, S*CH*$_2$), 115.6 [CH, d, $^2J_{CF}$ 23, aromatic *C*H, ArC(3′)], 122.0 [CH, d, $^3J_{CF}$ 8, aromatic

*C*H, ArC(2′)], 128.8, 129.0, 130.9, (3 × CH, 3 × aromatic *C*H), 128.0, 132.8, 133.4, 145.7 [4 × C, aromatic *C*, *C*(2)S or *C*(3)Cl], 159.1 (C, *C*O), 159.7 [*C*, d, $^{1}J_{CF}$ 245, aromatic *C*, ArC(4′)],; Exact mass calcd for $C_{17}H_{16}NO_2SClF$ $[M+H]^+$, 352.0574. Found 352.0584; 352 ($[M+H]^+$, 100%), 91 ($C_7H_7^+$, 4%).

4.36. *N*-Benzyl-3-morpholino-2-(benzylsulfonyl)propenamide 4c

A solution of *m*-CPBA (0.51 g of 65% pure material, 1.9 mmol) in dichloromethane (5 mL) was added dropwise to a stirred solution of the sulfoxide *N*-benzyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **2c** (0.32 g, 1.0 mmol) in dichloromethane (15 mL). Following stirring at room temperature for 24 h, TLC analysis showed that all the sulfoxide starting material had been consumed and morpholine (0.33 mL, 3.8 mmol) was added directly to the reaction mixture. The reaction progress was monitored by TLC, which indicated that the reaction was complete after 5 min and the work-up involved washing with water (3 × 10 mL) and brine (10 mL). Following drying using anhydrous magnesium sulfate and evaporation of the solvent at reduced pressure, the crude sulfone **4c** was obtained as a brown oil. This was purified by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 20–50% ethyl acetate) and the pure sulfone **4c** (0.16 g, 42%) was isolated as a white solid, mp 177–180 °C; ($C_{21}H_{24}N_2O_4S$ requires C, 62.98; H, 6.04; N, 6.99; S, 8.01. Found: C, 62.67; H, 5.96; N, 6.72; S, 8.20.); ν_{max}/cm^{-1} (KBr) 3378 (NH), 3028 (CH), 2968 (CH), 1640 (CO), 1595 (NH bend), 1508, 1439 (CN stretch), 1352 (asymmetric SO_2 stretch), 1120 (symmetric SO_2 stretch); δ_H (300 MHz, $CDCl_3$) 3.29–3.36 [4H, m, NC(2′)H_2 and NC(6′)H_2], 3.64–3.70 [4H, m, OC(3′)H_2 and OC(5′)H_2], 4.14 (2H, s, SCH_2), 4.44 (2H, d, *J* 6.0, CH_2NH), 6.83 [1H, s, C(3)*H*N=], 7.22–7.37 (10H, m, Ar*H*), 7.59 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 42.7 (CH_2, *C*H_2NH), 51.1 [CH_2, br, NC(2′)H_2 and NC(6′)H_2], 60.2 (CH_2, SCH_2), 65.5 [CH_2, OC(3′)H_2 and OC(5′)H_2], 96.8 [C, *C*(2)S], 126.5, 126.8, 127.4, 127.5, 127.7, 130.1 (CH, aromatic *C*H), 137.3 (C, aromatic *C*), 151.5 [CH, *C*(3)HN=], 161.3 (C, *C*O); *m*/*z* (ESI) 401 ($[M+H]^+$, 100%).

4.37. *N*-Benzyl-3-morpholino-2-(benzylsulfonyl)propenamide 4a

This was prepared following the procedure outlined for **4c** using *m*-CPBA (0.51 g of 65% pure material, 1.9 mmol) in dichloromethane (5 mL) and *N*-4′-methylphenyl-*Z*-3-chloro-2-(phenylsulfinyl)propenamide (0.32 g, 1.0 mmol) in dichloromethane (15 mL) to give the crude sulfone as a brown oil. This was purified by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 20–50% ethyl acetate) and the pure sulfone (0.16 g, 42%) was isolated as a white solid; ν_{max}/cm^{-1} (KBr) 3346 (NH), 2964 (CH), 2920 (CH), 1661 (CO), 1597 (NH bend), 1515, 1445 (CN stretch), 1354 (asymmetric SO_2 stretch), 1136 (symmetric SO_2 stretch); δ_H (300 MHz, $CDCl_3$) 2.29 (3H, s, Ar-CH_3), 3.46–3.56 [4H, m, NC(2″)H_2 and NC(6″)H_2], 3.71–3.81 [4H, m, OC(3″)H_2 and OC(5″)H_2], 7.04–7.13 (2H, m, Ar*H*), 7.22–7.30 (2H, m, Ar*H*), 7.37–7.54 (3H, m, Ar*H*), 7.65 [1H, s, C(3)*H*N=], 7.78–7.85 (2H, m, Ar*H*), 8.98 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 20.9 (CH_3, Ar-*C*H_3), 52.4 [CH_2, br, NC(2″)H_2 and NC(6″)H_2], 66.4 [CH_2, OC(3″)H_2 and OC(5″)H_2], 101.6 [C, *C*(2)S], 120.3, 126.6, 129.1, 129.5, 132.6 (CH, aromatic *C*H), 134.0, 135.0, 142.1 (C, aromatic *C*), 151.7 [CH, *C*(3)HN=], 159.9 (C, *C*O); Exact mass calcd for $C_{20}H_{23}N_2O_4S$ $[M+H]^+$, 387.1379. Found 387.1384; 387 ($[M+H]^+$, 100%).

4.38. *N*-4′-Fluorophenyl-3-morpholino-2-(benzylsulfonyl)propenamide 4d

This was prepared following the procedure outlined for **4c** using *N*-4′-fluorophenyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **2d** (0.20 g, 0.6 mmol) in dichloromethane (15 mL) and *m*-CPBA (0.32 g of 65% pure material, 1.2 mmol) in dichloromethane (5 mL). Following stirring at room temperature for 24 h, morpholine (0.21 mL, 2.4 mmol) was added and TLC analysis showed that the reaction was complete after 10 min and the crude sulfone **4d** was obtained as an off-white solid. Following purification by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 5–40% ethyl acetate), the sulfone **4d** (0.10 g, 43%) was isolated as a white solid, mp 179–182 °C; ($C_{20}H_{21}FN_2O_4S$ requires C, 59.39; H, 5.23; N, 6.93; S, 7.93; F, 4.70. Found: C, 59.45; H, 5.38; N, 6.57; S, 7.56; F, 4.69.); ν_{max}/cm^{-1} (KBr) 3335 (NH), 2929 (CH), 1652 (CO), 1615, 1534 (NH bend), 1508, 1407 (CN stretch), 1362 (asymmetric SO_2 stretch), 1114 (symmetric SO_2 stretch); δ_H (300 MHz, $CDCl_3$) 3.22–3.44 [4H, m, NC(2′)H_2 and NC(6′)H_2], 3.54–3.76 [4H, m, OC(3′)H_2 and OC(5′)H_2], 4.37 (2H, s, SCH_2), 6.85 [1H, s, C(3)*H*N=], 6.95 [2H, overlapping dd (appears as a triplet), *J* 8.7, 8.7, ArC(3′)*H*], 7.20–7.55 (7H, m, Ar*H*), 9.22 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 52.4 [CH_2, br, NC(2′)H_2 and NC(6′)H_2], 62.5 (CH_2, SCH_2), 66.8 [CH_2, OC(3′)H_2 and OC(5′)H_2], 98.1 [C, *C*(2)S], 115.8 [CH, d, $^{2}J_{CF}$ 22, aromatic *C*H, ArC(3′)], 121.7 [CH, d, $^{3}J_{CF}$ 8, aromatic *C*H, ArC(2′)], 128.9, 129.0, (CH, aromatic *C*H), 129.5 (C, aromatic *C*), 131.5 (CH, aromatic *C*H), 134.3 (C, aromatic *C*), 153.5 [CH, *C*(3)HN=], 158.0/161.3 [C, d, $^{1}J_{CF}$ 243, aromatic *C*, ArC(4′)], 161.1 (C, *C*O); *m*/*z* (ESI) 427 ($[M+Na]^+$, 100%), 91 ($C_7H_7^+$, 99%).

4.39. *N*-*n*-Butyl-3-morpholino-2-(benzylsulfonyl)propenamide 4e

This was synthesised as described for **4c** using *N*-*n*-butyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **2e** (0.10 g, 0.3 mmol) in dichloromethane (15 mL) and *m*-CPBA (0.18 g of 65% pure material, 0.7 mmol) in dichloromethane (5 mL). Morpholine (0.12 mL, 1.3 mmol) was added to the reaction mixture after stirring at room temperature for 24 h. TLC analysis indicated that the reaction was complete after 10 min and following the work-up, the crude sulfone was obtained as a yellow solid. Following purification by column chromatography on silica gel using hexane/ethyl acetate (60:40) as eluent, the sulfone **4e** (0.08 g, 63%) was isolated as a white solid, mp 116–119 °C; ν_{max}/cm^{-1} (KBr) 3347 (NH), 2922 (CH), 1635 (CO), 1594 (NH bend), 1514, 1436 (CN stretch), 1351 (asymmetric SO_2 stretch), 1120 (symmetric SO_2 stretch); δ_H (300 MHz, $CDCl_3$) 0.94 [3H, t, *J* 7.3, C(4′)H_3], 1.32–1.46 [4H, m, C(3′)H_2 and C(2′)H_2], 3.24 (2H, m, CH_2NH), 3.28–3.37 [4H, m, NC(2″)H_2 and NC(6″)H_2], 3.65–3.71 [4H, m, OC(3″)H_2 and OC(5″)H_2], 4.24 (2H, s, SCH_2), 6.80 [1H, s, C(3)*H*N=], 7.18 (1H, br s, N*H*), 7.21–7.38 (5H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 14.2 [CH_3, *C*(4′)H_3], 20.6 [CH_2, *C*(3′)H_2], 32.0 [CH_2, *C*(2′)H_2], 39.9 (CH_2, *C*H_2NH), 52.5 [CH_2, br, NC(2″)H_2 and NC(6″)H_2], 61.6 (CH_2, SCH_2), 66.9 [CH_2, OC(3″)H_2 and OC(5″)H_2], 98.4 [C, *C*(2)S], 128.8, 128.9 (CH, aromatic *C*H), 129.6 (C, aromatic *C*), 131.6 (CH, aromatic *C*H), 152.6 [CH, *C*(3)HN=], 162.8 (C, *C*O); Exact mass calcd for $C_{18}H_{26}N_2O_4SNa$ $[M+Na]^+$, 389.1511. Found 389.1506; 389 ($[M+Na]^+$, 100%), 91 ($C_7H_7^+$, 89%).

4.40. *N*-4′-Methylphenyl-3-morpholino-2-(benzylsulfonyl)propenamide 4f

This was prepared following the procedure outlined for **4c** using *N*-4′-methylphenyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **2f** (0.20 g, 0.6 mmol) in dichloromethane (15 mL) and *m*-CPBA (0.32 g of 65% pure material, 1.2 mmol) in dichloromethane (5 mL). Following stirring at room temperature for 24 h, morpholine (0.21 mL, 2.4 mmol) was added to the reaction mixture and TLC analysis showed that the reaction was complete 5 min after the addition. The crude sulfone was obtained as a brown solid after

the work-up and this was then purified by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 20–50% ethyl acetate) to give the pure sulfone **4f** (0.14 g, 56%) as a white solid, mp 154–156 °C; ν_{max}/cm^{-1} (KBr) 3337 (NH), 3032 (CH), 1651 (CO), 1613, 1526, 1406, 1359 (asymmetric SO_2 stretch), 1120 (symmetric SO_2 stretch); δ_H (300 MHz, $CDCl_3$) 2.33 (3H, s, Ar-C*H*$_3$), 3.32–3.44 [4H, m, NC(2″)H_2 and NC(6″)H_2], 3.63–3.75 [4H, m, OC(3″)H_2 and OC(5″)H_2], 4.30 (2H, s, SCH_2), 6.88 [1H, s, C(3)*H*N=], 7.14 (2H, m, Ar*H*), 7.24–7.50 (7H, m, Ar*H*), 9.02 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 20.9 (CH_3, Ar-*C*H_3), 52.6 [CH_2, br, NC(2″)H_2 and NC(6″)H_2], 61.7 (CH_2, SCH_2), 66.5 [CH_2, OC(3″)H_2 and OC(5″)H_2], 98.0 [CH, *C*(2)S], 119.9, 128.5, 128.6 (CH, aromatic *C*H), 129.1 (C, aromatic *C*), 129.4, 131.1 (CH, aromatic *C*H), 134.0, 135.3 (C, aromatic *C*), 153.1 [CH, *C*(3)HN=], 160.3 (C, *C*O); Exact mass calcd for $C_{21}H_{24}N_2O_4SNa$ $[M+Na]^+$, 423.1354. Found 423.1346; 401 ($[M+H]^+$, 100%), 91 ($C_7H_7^+$, 18%).

4.41. *N*-Methyl-3-morpholino-2-(benzylsulfonyl)propenamide 4g

This was synthesised according to the procedure outlined for **4c** using *N*-methyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **2g** (0.21 g, 0.80 mmol) in dichloromethane (10 mL) and *m*-CPBA (0.43 g of 95% pure material, 2.4 mmol) in dichloromethane (5 mL). Morpholine (0.42 mL, 4.8 mmol) was added to the reaction solution following stirring at room temperature for 48 h. TLC analysis indicated that the reaction was complete after 5 min and the crude sulfone **4g** was obtained as an orange oil after the work-up. This was then purified by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 40–60% ethyl acetate) to give the pure sulfone **4g** (0.10 g, 38%) as a white solid, mp 130–132 °C; ($C_{15}H_{20}N_2O_4S$ requires C, 55.54; H, 6.21; N, 8.64; S, 9.88. Found: C, 55.40; H, 6.25; N, 8.64; S, 9.75.); ν_{max}/cm^{-1} (film) 3323 (NH), 2996 (CH), 1652 (CO), 1548 (NH bend), 1495, 1410 (CN stretch), 1310 (asymmetric SO_2 stretch), 1110 (symmetric SO_2 stretch); δ_H (300 MHz, $CDCl_3$) 2.77 (3H, d, *J* 4.8, C*H*$_3$NH), 3.30-3.42 [4H, m, NC(2′)H_2 and NC(6′)H_2], 3.64–3.73 [4H, m, OC(3′)H_2 and OC(5′)H_2], 4.25 (2H, s, SCH_2), 6.82 [1H, s, C(3)*H*N=], 7.14 (1H, br s, N*H*), 7.31–7.39 (5H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 26.9 (CH_3, *C*H_3NH), 52.4 [CH_2, br, NC(2′)H_2 and NC(6′)H_2], 61.7 (CH_2, SCH_2), 66.9 [CH_2, OC(3′)H_2 and OC(5′)H_2], 98.3 [C, *C*(2)S], 128.9, 129.0 (CH, aromatic *C*H), 129.6 (C, aromatic *C*), 131.6 (CH, aromatic *C*H), 152.8 [CH, *C*(3)HN=], 163.5 (C, *C*O); Exact mass calcd for $C_{15}H_{21}N_2O_4S$ $[M+H]^+$, 325.1222. Found 325.1213; 325.3 ($[M+H]^+$, 100%).

4.42. *N*-Phenyl-3-morpholino-2-(benzylsulfonyl)propenamide 4h

This was prepared following the procedure described for **4c** using *N*-phenyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **2h** (0.30 g, 0.9 mmol) in dichloromethane (20 mL) and *m*-CPBA (0.50 g of 65% pure material, 1.9 mmol) in dichloromethane (15 mL). Following stirring at room temperature for 24 h, TLC analysis indicated that there was some starting material still present and so a further 2 equiv of *m*-CPBA (0.50 g of 65% pure material, 1.9 mmol) was added to the reaction mixture. After stirring for a further 24 h all traces of the starting material had disappeared and morpholine (0.50 mL, 5.6 mmol) was added. TLC analysis indicated that this reaction was complete after 5 min and following the work-up the crude sulfone was obtained as an orange solid. This was then purified by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 20–60% ethyl acetate) to give the pure sulfone **4h** (0.19 g, 56%) as a white solid, mp 129–132 °C; ($C_{20}H_{22}N_2O_4S$ requires C, 62.16; H, 5.74; N, 7.25; S, 8.30. Found: C, 62.23; H, 5.76; N, 7.08; S, 7.98.); ν_{max}/cm^{-1} (KBr) 3303 (NH), 2960 (CH), 1655 (CO), 1607, 1531 (NH bend), 1499, 1407 (CN stretch), 1314 (asymmetric SO_2 stretch), 1111 (symmetric SO_2 stretch); δ_H (300 MHz, $CDCl_3$) 3.23–3.45 [4H, m, NC(2′)H_2 and NC(6′)H_2]. 3.55–3.94 [4H, m, OC(3′)H_2 and OC(5′)H_2], 4.31 (2H, s, SCH_2), 6.94 [1H, s, C(3)*H*N=], 7.05–7.64 (10H, m, Ar*H*), 9.10 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 52.7 [CH_2, br, NC(2′)H_2 and NC(6′)H_2], 62.2 (CH_2, SCH_2), 66.9 [CH_2, OC(3′)H_2 and OC(5′)H_2], 98.4 [C, *C*(2)S], 120.2, 124.7, 128.5, 128.9 (CH, aromatic *C*H), 129.2 (C, aromatic *C*), 129.3, 131.5 (CH, aromatic *C*H), 138.3 (C, aromatic *C*), 153.7 [CH, *C*(3)HN=], 160.8 (C, *C*O). Exact mass calcd for $C_{20}H_{23}N_2O_4S$ $[M+H]^+$, 387.1379. Found 387.1379; 387.2 ($[M+H]^+$, 100%).

4.43. 3-Morpholino-2-(benzylsulfonyl)propenamide 4i

This was synthesised according to the procedure outlined for **4c** using *Z*-3-chloro-2-(benzylsulfinyl)propenamide **2i** (0.08 g, 0.4 mmol) in dichloromethane (10 mL) and *m*-CPBA (0.18 g of 65% pure material, 0.7 mmol) in dichloromethane (5 mL). Following stirring at room temperature for 24 h, TLC analysis indicated that there was some starting material still present and so a further 2 equiv of *m*-CPBA (0.18 g of 65% pure material, 0.7 mmol) was added to the reaction mixture. After stirring for a further 24 h all traces of the starting material had disappeared and morpholine (0.12 mL, 1.4 mmol) was added. TLC analysis indicated that this reaction was complete after 5 min and following the work-up the crude sulfone was obtained as an orange solid. This was then purified by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 20–100% ethyl acetate) to give the pure sulfone **4i** (0.04 g, 37%) as a white solid, mp 178–179 °C; ν_{max}/cm^{-1} (KBr) 3440 (NH), 3168 (NH), 2981 (CH), 1646 (CO), 1579 (NH bend), 1495, 1410 (CN stretch), 1324 (asymmetric SO_2 stretch), 1116 (symmetric SO_2 stretch); δ_H (300 MHz, $CDCl_3$) 3.21–3.46 [4H, m, NC(2′)H_2 and NC(6′)H_2], 3.55–3.80 [4H, m, OC(3′)H_2 and OC(5′)H_2], 4.32 (2H, s, SCH_2), 5.59 (1H, br s, one of NH_2), 6.83 [1H, s, C(3)*H*N=], 7.19 (1H, br s, one of NH_2), 7.26–7.46 (5H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 53.0 [CH_2, br signal, NC(2′)H_2 and NC(6′)H_2], 61.3 (CH_2, SCH_2), 61.9 [CH_2, OC(3′)H_2 and OC(5′)H_2], 97.2 [C, *C*(2)S], 128.9, 129.0 (CH, aromatic *C*H), 129.6 (C, aromatic *C*), 131.5 (CH, aromatic *C*H), 154.4 [CH, *C*(3)HN=], 164.5 (C, *C*O); Exact mass calcd for $C_{14}H_{19}N_2O_4S$ $[M+H]^+$, 311.1066. Found 311.1070; 311 ($[M+H]^+$, 50%), 91 ($C_7H_7^+$, 26%).

4.44. *N*-Benzyl-3-morpholino-2-(butylsulfonyl)propenamide 4j

This was prepared following the procedure outlined for **4c** using *N*-benzyl-*Z*-3-chloro-2-(butylsulfinyl)propenamide **2j** (0.25 g, 0.85 mmol) in dichloromethane (15 mL) and *m*-CPBA (0.90 g of 65% pure material, 3.38 mmol) in dichloromethane (5 mL). Following stirring at room temperature for 24 h, morpholine (0.60 mL, 6.80 mmol) was added and TLC analysis showed that the reaction was complete after 10 min and the crude sulfone was obtained as an orange oil. Following purification by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 10–60% ethyl acetate), the sulfone **4j** (0.10 g, 38%) was isolated as a white solid, mp 139–141 °C; ($C_{18}H_{26}N_2O_4S$ requires C, 58.99; H, 7.15; N, 7.64; S, 8.75. Found: C, 58.72; H, 7.07; N, 7.59; S, 8.49.); ν_{max}/cm^{-1} (KBr) 3379 (NH), 2971 (CH), 1642 (CO), 1593 (NH bend), 1505, 1351 (asymmetric SO_2 stretch), 1119 (symmetric SO_2 stretch); δ_H (300 MHz, $CDCl_3$) 0.86 [3H, t, *J* 7.4, C(4′)H_3], 1.24–1.34 [2H, m, C(3′)H_2], 1.49–1.69 [2H, m, C(2′)H_2], 2.85–2.90 (2H, m, SCH_2), 3.44–3.47 [4H, m, NC(2′)H_2 and NC(6′)H_2], 3.73–3.76 [4H, m, OC(3′)H_2 and OC(5′)H_2], 4.48 (2H, d, *J* 6.1, CH_2NH), 7.22–7.55 [6H, m, ArH and C(3)*H*N=], 7.62 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 13.9 [CH_3, *C*(4′)H_3], 21.8 [CH_2, *C*(3′)H_2], 25.3

[CH_2, $C(2')H_2$], 44.1 (CH_2, CH_2NH), 52.5 [CH_2, br, $NC(2')H_2$ and $NC(6')H_2$], 55.0 (CH_2, SCH_2), 66.8 [CH_2, $OC(3')H_2$ and $OC(5')H_2$], 99.7 [C, *C*(2)S], 127.9, 128.3, 129.1 (3 × CH, 3 × aromatic *C*H), 138.6 (C, aromatic *C*), 151.9 [CH, *C*(3)HN=], 162.8 (C, *C*O); *m*/*z* (ESI) 367 ([M+H]$^+$, 100%).

4.45. *N*-4′-Methylphenyl-3-morpholino-2-(butylsulfonyl)propenamide 4k

This was prepared following the procedure outlined for **4c** using *N*-4′-methylphenyl-*Z*-3-chloro-2-(butylsulfinyl)propenamide **2k** (0.23 g, 0.75 mmol) in dichloromethane (15 mL) and *m*-CPBA (0.68 g of 65% pure material, 3.01 mmol) in dichloromethane (5 mL). Following stirring at room temperature for 24 h, morpholine (0.53 mL, 6.02 mmol) was added to the reaction mixture and TLC analysis showed that the reaction was complete 5 min after the addition. The crude sulfone was obtained as an orange oil after the work-up and this was then purified by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 10–40% ethyl acetate) to give the pure sulfone **4k** (0.11 g, 45%) as a pale orange oil; ν_{max}/cm^{-1} (NaCl) 3295 (NH), 2963 (CH), 1658 (CO), 1614, 1529, 1406, 1358 (asymmetric SO_2 stretch), 1120 (symmetric SO_2 stretch); δ_H (300 MHz, $CDCl_3$) 0.88 [3H, t, *J* 7.1, $C(4')H_3$], 1.33–1.49 [2H, m, $C(3')H_2$], 1.67–1.82 [2H, m, $C(2')H_2$], 2.32 (3H, s, Ar-CH_3), 3.08 (2H, t, *J* 8.1, SCH_2), 3.43–3.57 [4H, m, $NC(2')H_2$ and $NC(6')H_2$], 3.69–3.84 [4H, m, $OC(3')H_2$ and $OC(5')H_2$], 7.14 (2H, d, *J* 8.4, Ar*H*), 7.38 [1H, s, C(3)*H*N=], 7.42 (2H, d, *J* 8.4, Ar*H*), 9.02 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 13.9 [CH_3, $C(4')H_3$], 21.3 (CH_3, Ar-CH_3), 21.9 [CH_2, $C(3')H_2$], 25.4 [CH_2, $C(2')H_2$], 52.7 [CH_2, br, $NC(2'')H_2$ and $NC(6'')H_2$], 55.4 (CH_2, SCH_2), 66.8 [CH_2, $OC(3'')H_2$ and $OC(5'')H_2$], 100.0 [CH, *C*(2)S], 120.4, 129.9 (2 × CH, 2 × aromatic *C*H), 134.5, 135.6 (2 × C, 2 × aromatic *C*), 152.5 [CH, *C*(3)HN=], 160.8 (C, *C*O).

4.46. *N*-Phenyl-3-morpholino-2-(benzylsulfonyl)propenamide 4l

This was prepared following the procedure described for **4c** using *N*-phenyl-*Z*-3-chloro-2-(butylsulfinyl)propenamide **2l** (0.30 g, 1.07 mmol) in dichloromethane (15 mL) and *m*-CPBA (0.96 g of 65% pure material, 4.26 mmol) in dichloromethane (5 mL). Following stirring at room temperature for 48 h, morpholine (0.75 mL, 8.56 mmol) was added. TLC analysis indicated that this reaction was complete after 5 min and following the work-up the crude sulfone was obtained as an orange solid. This was then purified by column chromatography on silica gel using hexane/ethyl acetate as eluent (gradient elution 10–40% ethyl acetate) to give the pure sulfone **4l** (0.18 g, 54%) as a colourless oil; ν_{max}/cm^{-1} (NaCl) 3297 (NH), 2962 (CH), 1656 (CO), 1614, 1536, 1443, 1357 (asymmetric SO_2 stretch), 1119 (symmetric SO_2 stretch); δ_H (300 MHz, $CDCl_3$) 0.91 [3H, t, *J* 7.4, $C(4')H_3$], 1.33–1.51 [2H, m, $C(3')H_2$], 1.64–1.83 [2H, m, $C(2')H_2$], 3.03–3.18 (2H, m, SCH_2), 3.41–3.59 [4H, m, $NC(2')H_2$ and $NC(6')H_2$], 3.66–3.86 [4H, m, $OC(3')H_2$ and $OC(5')H_2$], 7.00–7.14 (1H, m, Ar*H*), 7.22–7.43 [3H, m, Ar*H* and C(3)*H*N=], 7.45–7.63 (2H, m, Ar*H*), 9.12 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 14.0 [CH_3, $C(4')H_3$], 21.9 [CH_2, $C(3')H_2$], 25.4 [CH_2, $C(2')H_2$], 52.6 [CH_2, br, $NC(2'')H_2$ and $NC(6'')H_2$], 55.6 (CH_2, SCH_2), 66.8 [CH_2, $OC(3'')H_2$ and $OC(5'')H_2$], 100.0 [CH, *C*(2)S], 120.2, 124.8, 129.4 (3 × CH, 3 × aromatic *C*H), 138.2, (C, aromatic *C*), 152.4 [CH, *C*(3)HN=], 161.1 (C, *C*O).

4.47. Attempted asymmetric oxidation of 1a to 2a: Modena procedure, 1,2-dichloroethane as solvent

Freshly distilled titanium isopropoxide (0.10 mL, 0.33 mmol) was added to a solution of (+)-DET (0.22 mL, 1.32 mmol) in 1,2-dichloroethane (Aldrich reagent grade, 3 mL) in a round-bottomed flask under a nitrogen atmosphere. The reaction solution was cooled to −20 °C by careful addition of dry ice to an acetone bath. Cumene hydroperoxide (0.12 mL, 0.66 mmol) was added before the β-chloroacrylamide **1a** (100 mg, 0.33 mmol) was added as a solution in 1,2-dichloroethane (1 mL). The reaction solution was maintained at −20 °C for 1 h before it was transferred to the freezer for 18 h when it was washed with a 5% aqueous solution of sodium sulfite (3 × 5 mL), water (10 mL) and brine (10 mL), dried and concentrated at reduced pressure to give the crude product mixture. ^{1}H NMR spectroscopy (60 MHz) of this material showed no conversion of the β-chloroacrylamide **1a** to the sulfoxide **2a**.

4.48. Attempted asymmetric oxidation of 1a to 2a: Modena procedure, toluene as solvent

Freshly distilled titanium isopropoxide (0.10 mL, 0.33 mmol) was added to a solution of (+)-DET (0.22 mL, 1.32 mmol) in freshly distilled toluene (3 mL) in a round-bottomed flask under a nitrogen atmosphere. The reaction solution was cooled to −20 °C by careful addition of dry ice to an acetone bath. Cumene hydroperoxide (0.12 mL, 0.66 mmol) was added before the β-chloroacrylamide **1a** (100 mg, 0.33 mmol) was added as a solution in toluene (1 mL). The reaction solution was maintained at −20 °C for 1 h before it was transferred to the freezer for 18 h when it was washed with a 5% aqueous solution of sodium sulfite (3 × 5 mL), water (10 mL) and brine (10 mL), dried and concentrated at reduced pressure to give the crude product mixture. ^{1}H NMR spectroscopy (60 MHz) of this material showed no conversion of the β-chloroacrylamide **1a** to the sulfoxide **2a**.

4.49. Oxidations using in situ generation of oxaziridines

4.49.1. Attempted oxidation of *N*-4′-methylphenyl-*Z*-3-chloro-2-(phenylthio)propenamide 1a with (+)-[(7,7-dichlorocamphoryl)-sulfonyl]imine 6b

The β-chloroacrylamide **1a** (50 mg, 0.17 mmol) was treated with (+)-[(7,7-dichlorocamphoryl)sulfonyl]imine **6b** (46 mg, 0.17 mmol) and hydrogen peroxide (0.08 mL of 30% aqueous solution, 0.66 mmol) in DCM (3 mL) as outlined by Page et al.[42] for 9 days at room temperature. Following work-up, ^{1}H NMR spectroscopy (270 MHz) showed that no oxidation had occurred.

4.49.2. Attempted oxidation of *N*-4′-fluorophenyl-*Z*-3-chloro-2-(*n*-butylthio)propenamide 1j with (+)-[(7,7-dichlorocamphoryl)-sulfonyl]imine 6b

The β-chloroacrylamide **1j** (50 mg, 0.17 mmol) was treated with (+)-[(7,7-dichlorocamphoryl)sulfonyl]imine **6b** (49 mg, 0.17 mmol) and hydrogen peroxide (0.09 mL of 30% aqueous solution, 0.70 mmol) in DCM (3 mL) as outlined by Page et al.[42] for 9 days at room temperature. Following work-up, ^{1}H NMR spectroscopy (270 MHz) showed that no oxidation had occurred.

4.50. Oxidations using pre-prepared oxaziridines

4.50.1. Attempted oxidation of *N*-4′-methylphenyl-*Z*-3-chloro-2-(phenylthio)propenamide 1a with (+)-(2*R*,8a*S*)-10-camphorylsulfonyloxaziridine 6a

The β-chloroacrylamide **1a** (100 mg, 0.33 mmol) was treated with (+)-(2*R*,8a*S*)-10-camphorylsulfonyloxaziridine **6a** (76 mg, 0.33 mmol) in CCl_4 (1.60 mL) as outlined by Page et al.[42] for 5 days at room temperature. Following work-up, ^{1}H NMR spectroscopy (270 MHz) showed that no oxidation had occurred.

4.50.2. Attempted oxidation of *N*-4′-methylphenyl-*Z*-3-chloro-2-(*n*-butylthio)propenamide 1j with (+)-(2*R*,8a*S*)-10-camphorylsulfonyloxaziridine 6a

The β-chloroacrylamide **1j** (100 mg, 0.35 mmol) was treated with (+)-(2*R*,8a*S*)-10-camphorylsulfonyloxaziridine **6a** (80 mg, 0.35 mmol) in CCl_4 (1.60 mL) as outlined by Page et al.[42] for 5 days at room temperature. Following work-up, ^{1}H NMR spectroscopy (270 MHz) showed that no oxidation had occurred.

4.50.3. Attempted oxidation of *N*-4′-methylphenyl-*Z*-3-chloro-2-(phenylthio)propenamide 1a with (+)-(2*R*,8a*R**)-[(8,8-dichlorocamphoryl)sulfonyl]oxaziridine 6b

The β-chloroacrylamide **1a** (100 mg, 0.33 mmol) was treated with (+)-(2*R*,8a*R**)-[(8,8-dichlorocamphoryl)sulfonyl]oxaziridine **OxDiCl** (98 mg, 0.33 mmol) in CCl_4 (2 mL) as outlined by Page et al.[42] for 5 days at room temperature. Following work-up, ^{1}H NMR spectroscopy (270 MHz) showed that no oxidation had occurred.

4.50.4. Attempted oxidation of *N*-4′-methylphenyl-*Z*-3-chloro-2-(*n*-butylthio)propenamide 1j with (+)-(2*R*,8a*R**)-[(8,8-dichlorocamphoryl)sulfonyl]oxaziridine 6b

The β-chloroacrylamide **1j** (100 mg, 0.35 mmol) was treated with (+)-(2*R*,8a*R**)-[(8,8-dichlorocamphoryl)sulfonyl]oxaziridine **6b** (105 mg, 0.35 mmol) in CCl_4 (2 mL) as outlined by Page et al.[42] for 5 days at room temperature. Following work-up, ^{1}H NMR spectroscopy (270 MHz) showed some oxidation had occurred. Chromatography on silica gel using ethyl acetate/hexane (10:90) as eluent gave the β-chloroacrylamide **1j** (55 mg) and the sulfoxide (−)-**2j** (22 mg, 21%) as a colourless solid with 29% ee. Spectral characteristics were as reported previously.

4.50.5. Attempted asymmetric oxidation of 1a using chloroperoxidase

The β-chloroacrylamide **1a** (127 mg, 0.42 mmol) was treated with hydrogen peroxide (0.07 mL of 30% aqueous solution, 0.63 mmol) in citrate buffer solution (45 mL, pH 4.8) in the presence of chloroperoxidase (250 units) as outlined by Colonna et al. After 24 h, the reaction was worked up as described by Colonna et al.[39]; ^{1}H NMR spectroscopy (60 MHz) of the reaction product showed that no oxidation had occurred.

4.51. Asymmetric oxidation of 1a to (−)-2a using the Kagan procedure

Freshly distilled titanium isopropoxide (bp 43–45 °C at 0.04 mm Hg) (0.10 mL, 0.33 mmol) was added to a solution of (+)-diethyl tartrate (bp 100 °C at 0.1 mm Hg) (0.11 mL, 0.66 mmol) in freshly double distilled (P_2O_5 and CaH_2) DCM (2.75 mL) in a round-bottomed flask under a nitrogen atmosphere. On addition of the $Ti(O^iPr)_4$, the reaction solution turned yellow. Water (6 μL, 0.33 mmol) was then added from a micro syringe as slowly as possible. On completion of the water addition, the reaction solution was stirred at room temperature for 25 min. A solution of the β-chloroacrylamide **1a** (200 mg, 0.66 mmol) in freshly double distilled DCM (1 mL) was added and the reaction solution cooled to −30 °C by careful addition of dry ice to an acetone bath. The reaction solution was maintained at −30 °C for 40 min, then cumene hydroperoxide (0.12 mL, 0.66 mmol) was added dropwise from a micro syringe. The reaction solution was stirred at −30 °C for 5 min, then the reaction flask was transferred to a freezer at −21 °C. After 18 h, the flask was removed from the freezer and the contents were allowed to warm to room temperature. Water (0.1 mL) was added and the solution stirred for 2 h, during which time a gel formed. The gel was removed by filtration through a bed of Celite, which was then washed with DCM to ensure complete recovery of the product (the total volume of DCM after washing was 100 mL). Aqueous NaOH (2 mL of 2 M solution) and brine (1 mL) were added and the reaction mixture was stirred for 90 min. At this point, more brine (50 mL) was added and the phases separated. The organic layer was washed with brine (50 mL), dried and evaporated at reduced pressure to give a mixture of the sulfoxide **2a** [46% conversion by ^{1}H NMR spectroscopy (60 MHz)], the β-chloroacrylamide **1a** (54%) and 2-phenylpropan-2-ol. The 2-phenylpropan-2-ol was removed by bulb-to-bulb distillation at reduced pressure (100 °C at 2 mm Hg). Following chromatography on silica gel using ethyl acetate/hexane (gradient elution 5–30% ethyl acetate) as eluent, the sulfoxide (−)-**2a** was recovered (62 mg, 30%) as a colourless solid with 12% ee (enantiomeric excess determined by HPLC on a chiral AS column using hexane/IPA 90:10 as mobile phase detected at λ 254 nm). The major enantiomer eluted before the minor. Spectral characteristics were as reported previously.

4.52. General Bolm procedure—room temperature

$VO(acac)_2$ (2.6 mg, 0.01 mmol) was added to a round-bottomed flask containing the ligand (0.015 mmol) in DCM (2 mL). The resulting solution was stirred at room temperature for 5 min, then a solution of the appropriate β-chloroacylamide (1 mmol) in DCM (2.00 mL) was added. Then H_2O_2 (0.13 mL, 30%, 1.1 mmol) was added to the resulting solution. The reaction mixture was then stirred at room temperature for a further 16 h. Water (5 mL) was added and the phases separated; the organic layer was washed with water (2 × 5 mL) and brine (5 mL), dried and concentrated at reduced pressure to the crude product. Following chromatography on silica gel using ethyl acetate and hexane (20:80), the sulfoxide was recovered. The enantiomeric excess was determined by chiral HPLC.

4.53. General Bolm procedure—low temperature

$VO(acac)_2$ (2.6 mg, 0.01 mmol) was added to a round-bottomed flask containing the appropriate ligand (0.015 mmol) in DCM (2 mL). The resulting solution was stirred at room temperature for 5 min, then a solution of the appropriate β-chloroacylamide (1 mmol) in DCM (2.00 mL) was added. The temperature was then lowered to the required value. H_2O_2 (0.13 mL, 30%, 1.1 mmol) was added to the resulting solution at this temperature. The reaction mixture was then stirred at this temperature for a further 16 h. Water (5 mL) was added and the phases separated; the organic layer was washed with water (2 × 5 mL) and brine (5 mL), dried and concentrated at reduced pressure to give the crude product. Following chromatography on silica gel using ethyl acetate and hexane, the sulfoxide was recovered. The enantiomeric excess was determined by chiral HPLC.

Note: a similar procedure was employed for reactions carried out at elevated temperatures, except in these experiments the H_2O_2 was added before heating commenced.

Details of the outcome of the Kagan and Bolm oxidations are summarised in Tables 3–6.

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