Title	Synthesis and stereoselective oxidation of α-Thio-ß-chloropropenyloxazolidin-2-ones
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Publication date	2010-11-08
Original Citation	KISSANE, M., MURPHY, M., LAWRENCE, S. E. & MAGUIRE, A. R. 2010. Synthesis and stereoselective oxidation of α-thio-ß-chloropropenyloxazolidin-2-ones. Tetrahedron: Asymmetry, 21, 2550-2558. doi: 10.1016/j.tetasy.2010.10.007
Type of publication	Article (peer-reviewed)
Link to publisher's version	10.1016/j.tetasy.2010.10.007
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Synthesis and Stereoselective Oxidation of α-Thio-β-Chloropropenyloxazolidin-2-ones

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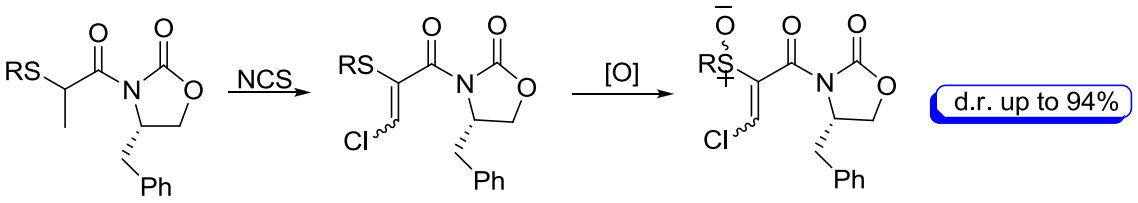


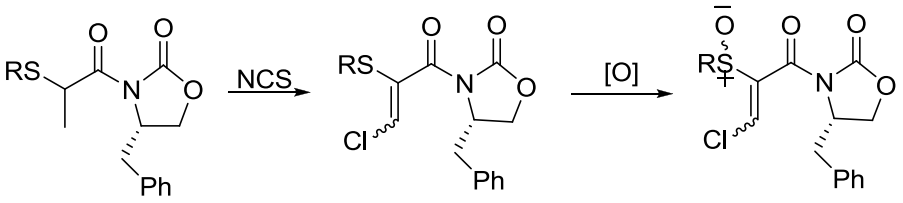
Abstract:

Investigation of the stereoselective reaction of α-thiopropanoyloxazolidin-2-ones with NCS to yield α-thio-β-chloropropenyloxazolidin-2-ones is described. Diastereoselective sulfur oxidation of the resulting α-thio-β-chloropropenyloxazolidin-2-ones is also discussed, with modest diastereocontrol achieved. However, through a combination of diastereoselective oxidation and subsequent kinetic resolution in the sulfoxide oxidation, diastereoselectivities of up to 94% de are achieved.

Introduction

We have recently reported the highly efficient and stereoselective transformation of α-thioamides, α-thioesters and α-thionitriles to the corresponding α-thio-β-chloroacrylamide, α-thio-β-chloroacrylate and α-thio-β-chloroacrylonitrile derivatives on treatment with NCS,[1-3] with the novel transformation proving particularly effective for the α-thioamide derivatives.

While amides have been employed as chiral auxiliaries in asymmetric synthesis with some success,[4] use of oxazolidinones as chiral auxiliaries has in many instances led to excellent relay of stereochemistry.[5-10] Chiral 2-oxazolidinones, first reported by Evans in 1981,[5] have proven to be highly versatile chiral auxiliaries, with high asymmetric induction achieved in alkylations, aminations, azidations, brominations, hydroxylations, aldol additions, Diels-Alder cycloadditions and conjugate reactions.[6-9] Therefore, we wished to extend this chlorination chemistry to α-thiopropanoyloxazolidin-2-ones, and explore the asymmetric induction in reactions of the resulting α-thio-β-chloropropenyloxazolidin-2-ones**,** focussing specifically on diastereoselective oxidation (Scheme 1). We have recently shown that with simple chiral amide auxiliaries, some, albeit modest, diastereocontrol is possible.[11] The diastereoselective sulfur oxidation of chiral *N*-arylthio and *N*-(alkylthio)oxazolidinones has been investigated by Evans using a range of achiral oxidising reagents.[10] Although the diastereoselectivity was poor, the diastereomers were easily separated by fractional crystallisation or chromatography and reacted readily with a variety of Grignard reagents to afford chiral sulfoxides.



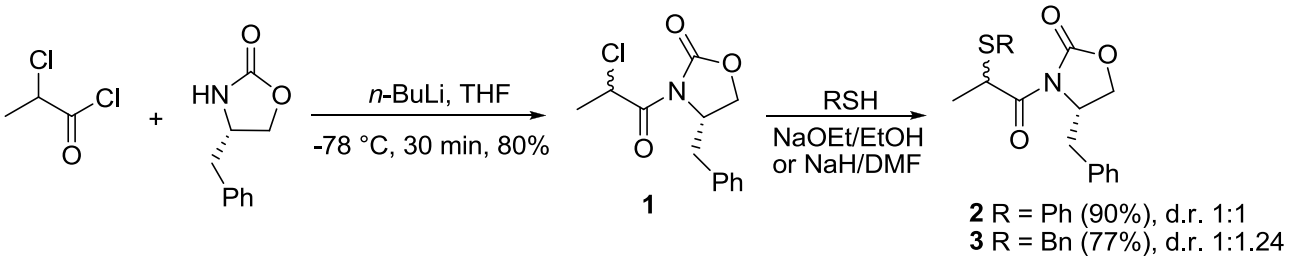
Scheme 1

Herein, the reactivity of α-thiopropanoyloxazolidin-2-ones with NCS is described. Diastereoselective sulfur oxidation of the resulting α-thio-β-chloropropenyloxazolidin-2-ones is also discussed.

Results and Discussion

Preparation of β-chloropropenyloxazolidin-2-ones

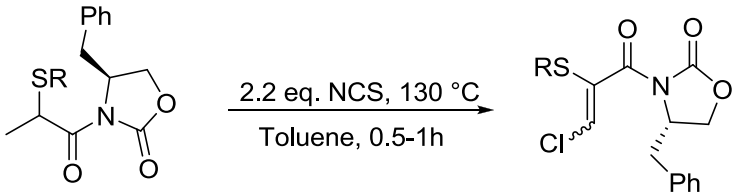
The α-thiopropanoyloxazolidin-2-ones were synthesised in two steps – the α-chloroamide **1** was first prepared by the method described by Evans and Gage in 80% yield as an equimolar mixture of diastereomers.[12] The α-phenylthiopropanoyloxazolidin-2-one **2** was prepared by sulfenylation of **1** by reaction in ethanol with the 1.1 equivalents of the freshly prepared salt of benzenethiol to produce **2** as an equimolar mixture of diastereomers in 90% yield. Synthesis of the α-benzylthiopropanoyloxazolidin-2-one **3** was initially attempted in a similar manner, however, in addition to nucleophilic displacement of the chloride group by the benzylthiolate anion, displacement of the oxazolidinone group by ethoxide also occurred. The α-benzylthiopropanoyloxazolidin-2-one **3** was subsequently prepared in 77% yield by reaction of **1** with 1.05 equivalents of sodium hydride and 1.05 equivalents of benzyl thiol in anhydrous DMF. The α-benzylthiopropanoyloxazolidin-2-one **3** was isolated as a 1 : 1.24 mixture of diastereomers.



Scheme 2

Investigation of the reaction of the α-thiopropanoyloxazolidin-2-ones **2** and **3** with NCS was then undertaken, with the results summarised in Table 1.

Table 1 Synthesis of β-chloroacrylamides bearing (4S)-benzyloxazolidin-2-one auxiliary



Sulfide	**R**	***Z*/*E***	**β-Cl**	**% yield**[a]
2[b]	Ph	*E*	*E*-**4**[c]	29[d]
		Z	*Z*-**5**[c]	22[d]

3[e]	Bn	*E*	*E*-**6**[f]	41

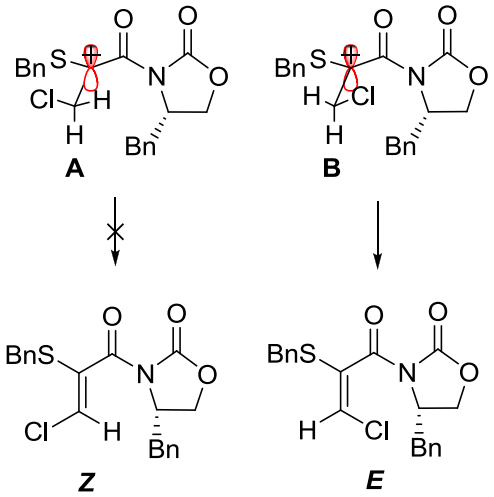
a) Yield after chromatography on silica gel.
b) Equimolar mixture of diastereomers.
c) Stereochemistry tentatively assigned.
d) Crude ratio of *E*-**5:** *Z*-**6** 1 : 1.05.
e) 1 : 1.24 mixture of diastereomers
f) The oxazolidine-2,4-dione **7** was also isolated in 9% yield.

Treatment of the α-phenylthiopropanoyloxazolidin-2-one **2** with 2.2 equivalents of NCS in toluene at 130 °C resulted in a complex mixture of products, from which the *E*- and *Z*-β-chloropropenyloxazolidin-2-ones *E*-**4** and *Z*-**5** were isolated following chromatographic purification in yields of 29 and 22% respectively. The stereochemistry of the *E*- and *Z*-isomers was assigned by X-ray analysis on the sulfoxide derivative **8a** (see below). While chlorination of primary and secondary α-thioamides with NCS proceeds in a highly stereoselective manner, with exclusive formation of the β-chloroacrylamides as the *Z*-stereoisomer, the absence of an amide hydrogen in tertiary amides for intramolecular hydrogen bonding to sulfur results in a change in conformation of the intermediate carbocation, and deprotonation to form either the *E*- or *Z*-isomer is possible.[3] Thus, the current work is consistent with this earlier observation, as the lack of a hydrogen for intramolecular bonding to sulfur in **2** leads to the subsequent formation of the α-phenylthio-β-chloroacryloyloxazolidin-2-ones as a mixture of *E*- and *Z*- isomers.

The α-benzylthiopropanoyloxazolidin-2-one **3** was then reacted under identical conditions (2.2 equivalents NCS, toluene, 130 °C), and a again a complex mixture of products was obtained from which the *E*-β-chloropropenyloxazolidin-2-one **6** was isolated in 41% yield. There was no evidence for the formation of the *Z*-isomer in the ^{1}H NMR spectrum of the crude product. The reaction of **3** was also conducted using 1.95 equivalents of NCS in toluene at 90 °C for one hour, and again the *Z*-isomer was not detected. On employment of these conditions, the ^{1}H NMR spectrum of the crude product contained a number of unassigned signals and lower yields were obtained for *E*-**6** (32−36%) than with the higher temperature.

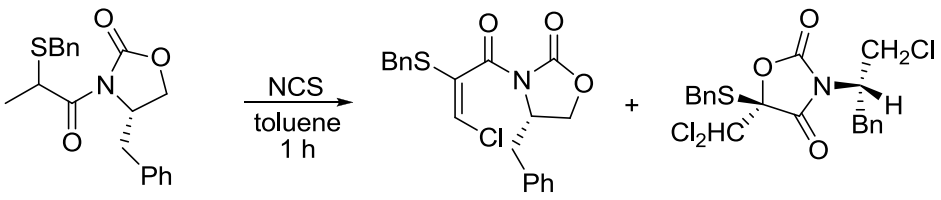
The absence of the *Z*-isomer on reaction of the α-benzylthiopropanoyloxazolidin-2-one **3** with NCS is in direct contrast to the results obtained with amides throughout this research programme and therefore is mechanistically significant.[3] The presence of the oxazolidinone moiety results in the sulfur-stabilised intermediate carbocation adopting a very different conformation to that of the primary and secondary propanamides, and it appears that

deprotonation from the sulfur-stabilised carbocation through conformation **B** to form the corresponding *E* isomer is energetically more favourable than elimination through conformation **A** (Scheme 3). An alternative explanation involves *E*-*Z* isomerisation in the β-chloropropenyloxazolidin-2-one **6**; earlier results with tertiary amides had suggested the possibility of interconversion in the benzylthio series.[2]



Scheme 3

In the ^{1}H NMR spectrum of the crude product from the reaction of the α-benzylthiopropanoyloxazolidin-2-one **3** with 2.2 equivalents of NCS, there was evidence for the presence of another compound (~30 mol%), a minor amount (9%) of which was recovered after chromatography. Elemental analysis indicated a molecular formula of $C_{20}H_{18}Cl_3NO_3S$ and the spectroscopic evidence suggested that the oxazolidinone was no longer intact; in particular, the CH_2O signal at δ_C 66ppm in the ^{13}C NMR spectrum of **3** now appeared at δ_C 42 ppm. Also, in the IR spectrum two carbonyl stretches were evident, with one of these carbonyl stretches at much higher frequency than that normally seen for the oxazolidinone derived β-chloroacrylamides (1827 and 1754 cm^{-1} *vs.* 1773 and 1674cm^{-1} for *E*-**6**). The structure was eventually confirmed as the oxazolidine-2,4-dione **7** by single crystal X-ray diffraction on a sample recrystallised from ethanol (Scheme 4 and Figure 1).



3 **6** **7**

Crude Product Ratios (2.2 eq., NCS, toluene, 130 °C)	1	0.43
Yields (2.2 eq., NCS, toluene, 130 °C)	41%	9%
Yields (1.95 eq. NCS, toluene, 90 °C)	32-36%	N.D.

Scheme 4

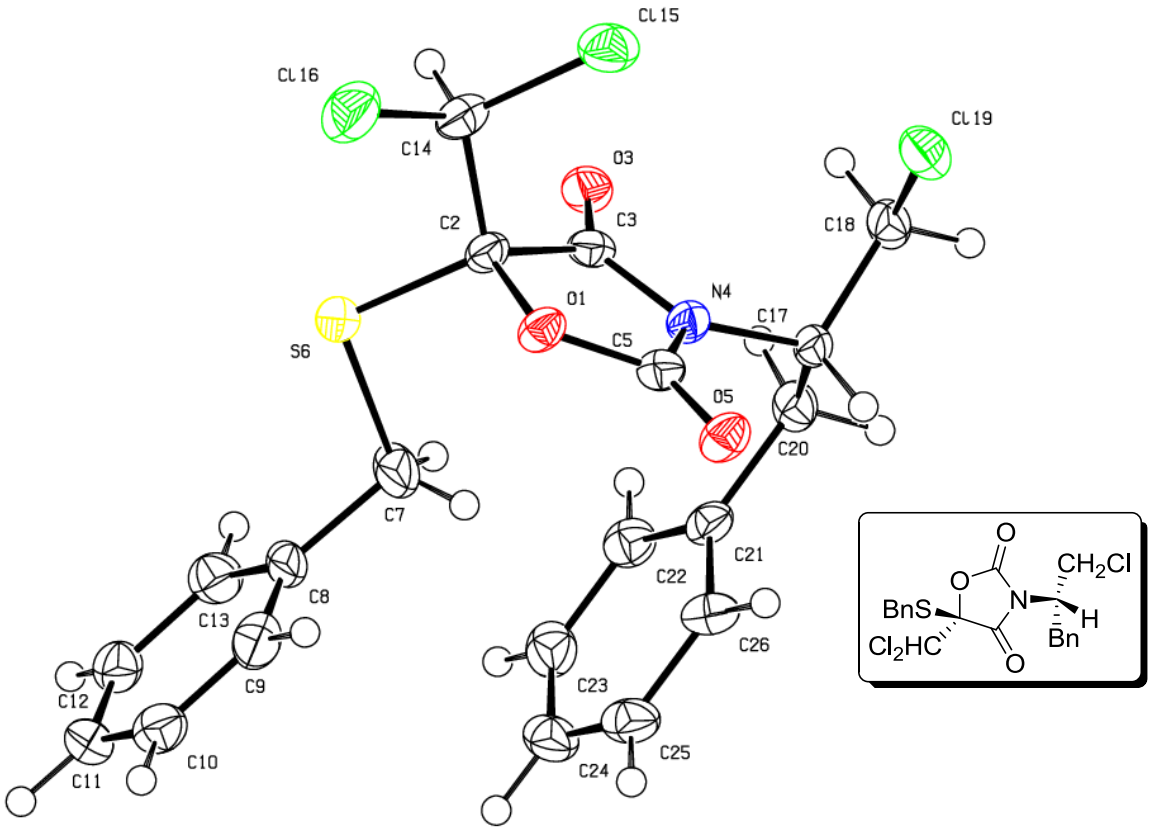
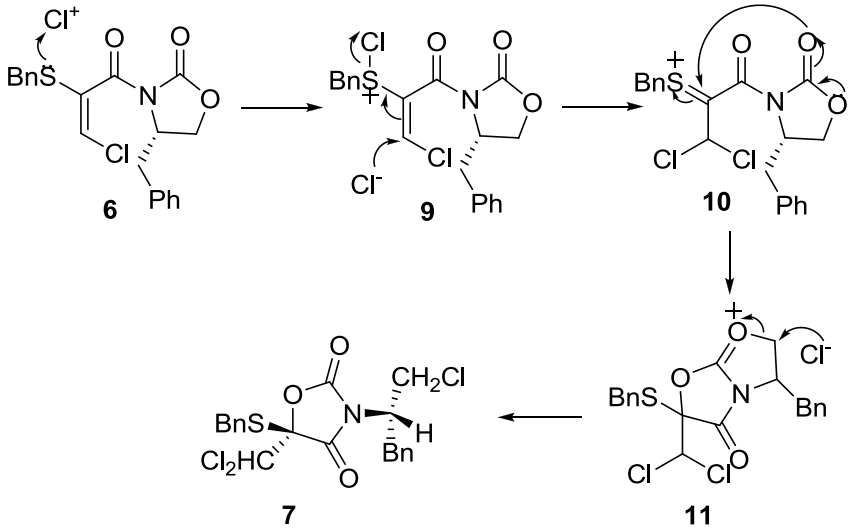


*Figure 1 ORTEP of **7** (Anisotropic displacement parameters are drawn at the 30% probability level)*

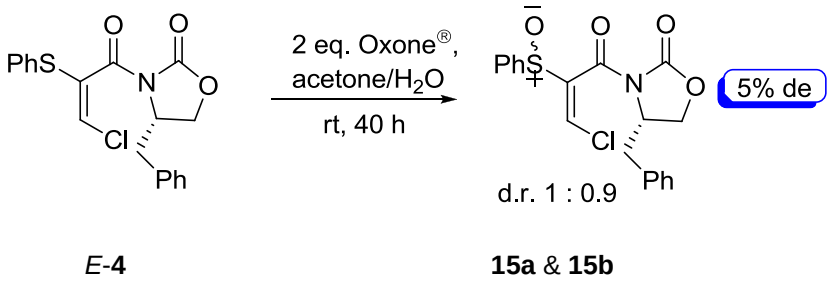
Scheme 5 summarises a proposed mechanistic pathway for the formation of the side-product **7**; as 2.2 equivalents of NCS are used in the reaction of **3**, overchlorination is possible. Thus, formation of the chlorosulfonium ion **9** is followed by nucleophilic addition of chloride to give the sulfur-stabilised carbocation **10**. The key step in the formation of the side-product **7** then involves intramolecular nucleophilic addition of oxazolidinone to the sulfur-stabilised carbocation **10** to form initially the intermediate cation **11**, followed by ring-opening through nucleophilic addition of chloride to form the oxazolidine-2,4-dione **7** (Scheme 5). Only a single isomer was detected, indicating selectivity in the diastereofacial approach to the carbocation in **10**. Oxazolidine-2,4-diones are biologically active compounds which have anticonvulsant properties.[13-15]



Scheme 5

Diastereoselective oxidation of β-chloropropenyloxazolidin-2-ones

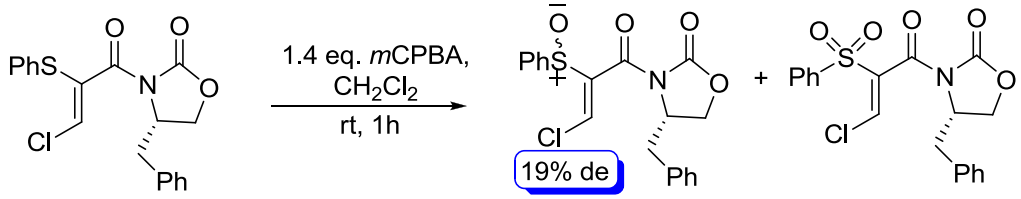
Having formed the β-chloropropenyloxazolidin-2-ones *E*-**4** and *Z*-**5** and *E*-**6**, the role of the oxazolidinone moiety in controlling the stereochemistry of oxidation at sulfur was next explored. We have recently shown that with simple chiral amide auxiliaries, some, albeit modest, diastereocontrol is possible.[11] Reaction of *E*-**4** with 2 equivalents of Oxone® led to a diastereomeric ratio of 1 : 0.9 of the resulting sulfoxides **15a** and **15b**, indicating that efficient asymmetric induction from the more remote oxazolidinone auxiliary was not feasible (in contrast to Evans' work where the oxazolidinone was bonded directly to the sulfide).[10] The diastereomers **15a** and **15b** were easily separated by chromatography on silica gel.



E-**4** **15a** & **15b**

Scheme 6

Oxidation of *Z*-**5** with 1.4 equivalents of *m*CPBA led to a 1 : 0.7 : 0.5 mixture of **16a**:**16b**:**17** sulfoxide diastereomers:sulfone (as determined by ^{1}H NMR spectroscopy) (Scheme 7). Chromatographic purification on silica gel led to the separation of the sulfoxides **16a** and **16b**, and a minor fraction (~7%) containing a 4.7 : 1 mixture of the sulfone **17**, and the minor sulfoxide **16b** was also isolated. Evidently, control of sulfide oxidations of the oxazolidinone derivatives is more challenging than in the corresponding amide derivatives, where chemoselective oxidation to the sulfoxide is easily achieved. Again, the diastereofacial discrimination is very small.



Z-**5** **16a** & **16b** **17**

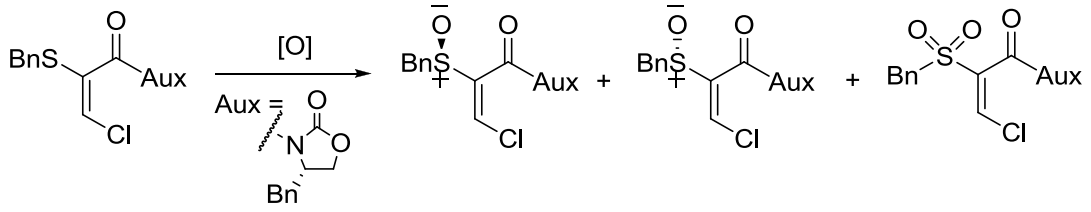
crude ratios **16a**:**16b**:**17** 1 : 0.7 : 0.5

Scheme 7

Clearly, retention of stereochemistry in the acrylamide is observed during the sulfur oxidation, with no evidence of *E*/*Z* isomerisation in the ^{1}H NMR spectra. This is consistent with the simpler β-chloroacrylamides.[16]

The diastereoselective sulfur oxidation of the *S*-benzyl substituted oxazolidinone derivative *E*-**6** was investigated under a variety of conditions, with the results summarised in Table 2.

*Table 2 Diastereoselective Oxidation of E-**6** with Subsequent Kinetic Resolution*



E-**6**	**8a**	**8b**	**18**

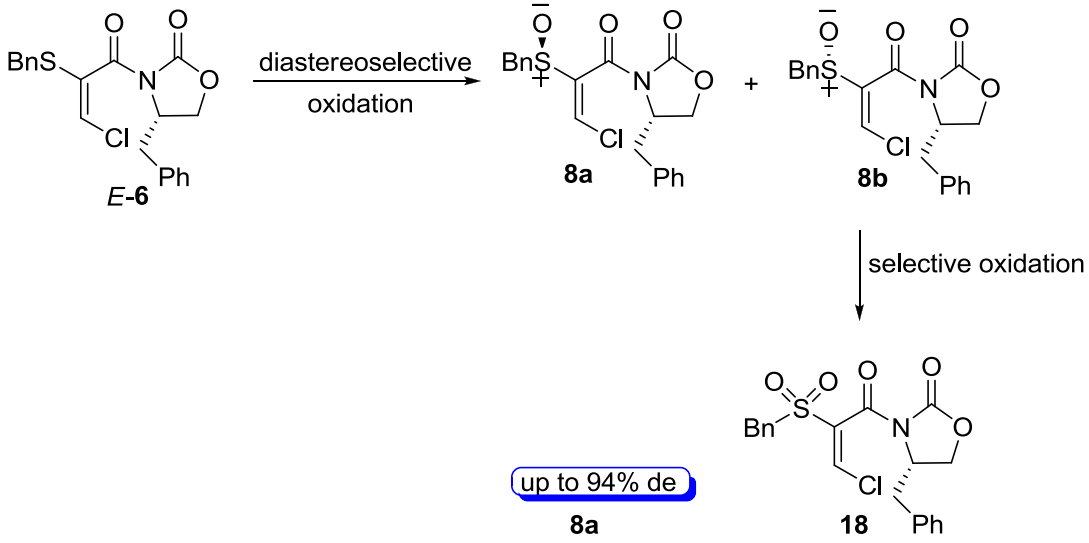
Conditions	**8a:8b:18**[a]	**% de**[a]
1.1 eq. *m*CPBA, CH_2Cl_2, rt, 16 h	1 : 0.5 : 0.03	36
3 eq. $NaIO_4$, MeOH/H_2O, rt, 5 d	1 : 0.4 : ND[b]	48
1 eq. Oxone®, acetone/H_2O, rt, 16 h	1 : 0.2 : 0.2	72
1.5 eq. Oxone®, acetone/H_2O, rt, 16 h	1 : 0.1 : 0.6	90
2 eq. Oxone®, acetone/H_2O, rt, 16 h	1 : 0.03 : 0.7	94

a) Estimated by integration of the ^{1}H NMR spectrum of the crude product.
b) ND = not detected.

Substituting the *S*-phenyl group in *E*-**4** and *Z*-**5** with the *S*-benzyl group in *E*-**6** results in improved diastereoselectivities. As indicated in Scheme 6 and Scheme 7, enhanced diastereoselectivity was observed starting from the *E* isomer, although the extent of this is very modest. Employment of *m*CPBA as oxidant afforded a 1:0.5:0.03 mixture of **8a:8b:18** sulfoxide diastereomers:sulfone, and an increase in the diastereoselectivity to 48% de was observed when sodium periodate was used. Oxone® proved to be the most expedient oxidant, with a diastereomeric excess of up to 94% achieved when two equivalents of Oxone® were employed. On closer examination of the Oxone® oxidation, it was clear that the initial diastereoselective oxidation was followed by selective oxidation of the minor sulfoxide **8b** to the sulfone **18**, leading to an enhancement of the diastereomeric excess of the sulfoxide (

Scheme 8); kinetic resolution has been shown to enhance the enantioselectivity in sulfur oxidation.[17-19] The sulfoxide **8a** was easily separated from the less polar sulfone **18** by chromatography on silica gel. From the product ratios summarised in Table 2, it is clear that oxidation of the minor diastereomer **8b** occurs selectively, but not exclusively, as the extent

of sulfone formation clearly indicates that **8a** also undergoes oxidation. Through appropriate choice of reaction conditions, the combination of diastereoselective oxidation and selective oxidation can lead to a very high diastereomeric purity in the sulfoxide **8a**, albeit in modest yield. Following chromatographic purification it is possible to obtain **8a** in diastereomerically pure form in 17% yield as the diastereomers **8a** and **8b** and the sulfone **18** are separable.



Scheme 8

The stereochemical assignment of **8a** was determined by single crystal X-ray diffraction after recrystallisation of a sample, which was diastereomerically pure by NMR spectroscopy, from dichloromethane and hexane, establishing the configuration at the sulfur centre as (*R*) (Figure 2). The X-ray crystallography also confirmed the *E* stereochemistry of the β-chloroacrylamide **8a** and hence of the sulfide precursor **6**.

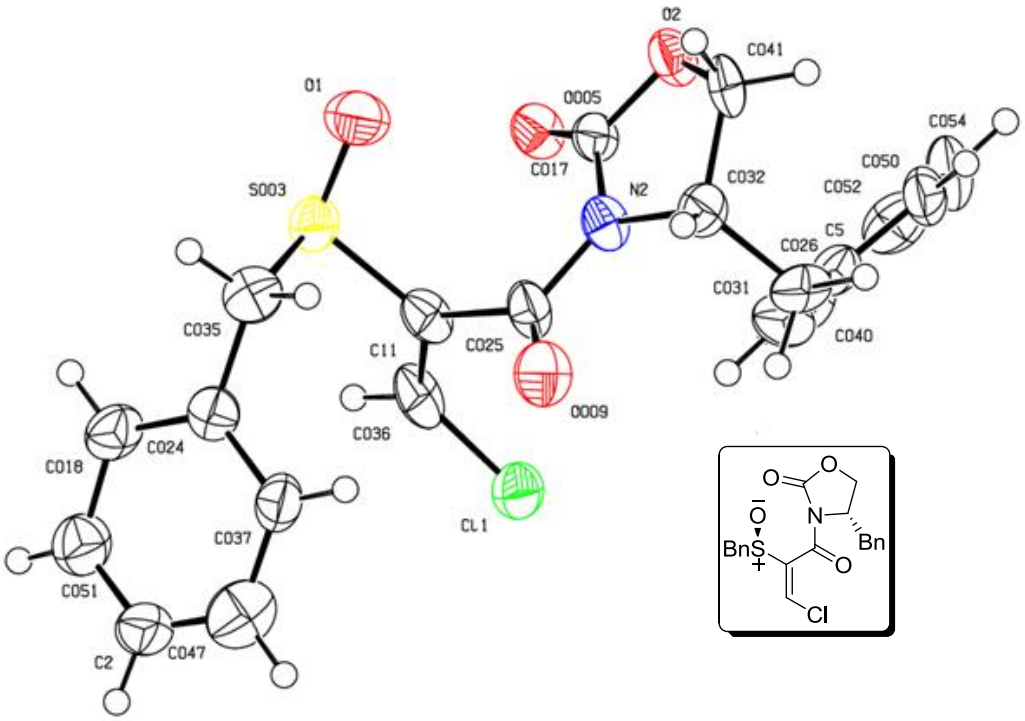


Figure 2

Examination of the crystal structure reveals that the electrophilic oxygen is delivered to the face opposite the benzyl group of the oxazolidinone as illustrated in Figure 3, assuming that the conformation is the same in the sulfide. This is consistent with the work conducted by Evans on the diastereoselective sulfur oxidation of chiral *N*-aryl and *N*-(alkylthio)oxazolidinones.[10] Investigation of the synthetic potential of the enantioenriched vinyl sulfoxides will be reported in due course, including efficient cleavage of the oxazolidinone moiety.

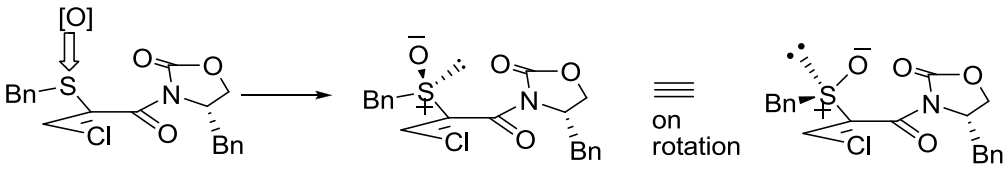


Figure 3

Conclusion

In summary, formation of the β-chloro-α,β-unsaturated derivatives of oxazolidinones is feasible, albeit with lower yields and reduced selectivity compared to studies with simple primary and secondary amides, and comparable in many ways to reactions with tertiary amides. Thus, we can access compounds which enable investigation of the efficiency of the transfer of stereoselectivity from the oxazolidinone auxiliary in reactions of the highly functionalised α,β-unsaturated system. While the diastereofacial discrimination is very small in the subsequent sulfur oxidations, selective oxidation of the minor sulfoxide **8b** to the sulfone **18** led to an enhancement of the diastereomeric excess of the sulfoxide, with diastereoselectivities of up to 94% de achieved.

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 sulphate. All commercial reagents, including *N*-chlorosuccinimide, were used without further purification. 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).

For optical rotations, concentrations (*c*) are expressed in g/100 mL. $[\alpha]_D^T$ is the specific rotation of a compound and is expressed in units of 10^{-1} deg cm^2 g^{-1}. Single crystal X-ray analysis calculations for **7** were made using the APEX2 software,[20] SHELXS, SHELXL[21] and PLATON[22] and for **8a** using CrysAlis,[23] SHELXS, SHELXL[21] and PLATON.[22] Diagrams

were prepared using PLATON.[22] Full structural data has been deposited at the Cambridge Crystallographic Data Centre. CCDC reference numbers 782119 and 782120.

(4*S*)-4-Benzyl-3-(2-chloropropanoyl)oxazolidin-2-one 1

Anhydrous tetrahydrofuran (30 mL) was added to a 3-necked round bottom flask containing (*S*)-4-benzyl-2-oxazolidinone (1.62 g, 9.0 mmol) under a nitrogen atmosphere. The resulting solution was cooled to −78 °C. *n*-Butyllithium (2.3 M in hexanes, 3.97 mL, 9.1 mmol) was then added to the reaction flask over 10 min. On completion of this addition, 2-chloropropionyl chloride (1.00 mL, 9.9 mmol) was added in one portion *via* syringe. The resulting solution was stirred for 30 min at −78 °C, and then allowed to warm slowly to room temperature over 30 min. The excess 2-chloropropionyl chloride was quenched by the addition of aqueous saturated ammonium chloride (10 mL). Most of the tetrahydrofuran and hexane was removed by concentration at reduced pressure (bath temperature 25-30 °C) and the resulting slurry was extracted with dichloromethane (2 × 10 mL). The combined organic extracts were washed with sodium hydroxide (1 M, 10 mL) and brine (10 mL), dried and concentrated under reduced pressure to give **1** as a white solid and an equimolar mixture of diastereomers (1.95 g, 80%), mp 80-82 °C; $[\alpha]_D^{20}$ +109.0 (*c* 1 in EtOH); ν_{max}/cm^{-1} (KBr) 3028 (CH), 1786 (CO oxazolidinone), 1708 (CO); δ_H (300 MHz, $CDCl_3$) 1.72, 1.74 [3H, contains 2 overlapping d, *J* 6.6, 6.6, C(3)H_3 of 2 diastereomers], 2.76-2.89 (1H, m, CH_AH$_B$Ph of 2 diastereomers), 3.26-3.35 (1H, m, CH$_A$$H_B$Ph of 2 diastereomers), 4.20-4.33 (2H, m, CH_2O of 2 diastereomers), 4.65-4.77 (1H, m, C*H*N of 2 diastereomers), 5.63-5.74 [1H, contains 2 overlapping q, *J* 6.9, 6.9, C(2)*H* of 2 diastereomers], 7.15-7.41 (5H, m, Ar*H* of 2 diastereomers); δ_C (150 MHz, $CDCl_3$) 20.4, 20.8 [2 × CH_3, *C*(3)H_3 of 2 diastereomers], 37.3, 37.8 (2 × CH_2, *C*H_2Ph of 2 diastereomers), 50.5, 50.8, 55.3, 55.7 [4 × CH, *C*(2)H & *C*HN of 2 diastereomers], 66.4, 66.6 (2 × CH_2, O*C*H_2 of 2 diastereomers), 127.5, 127.6, 129.1, 129.4,

129.5 (5 × CH, 5 × aromatic *C*H), 134.77, 134.83 (2 × C, 2 × aromatic *C*), 152.5, 152.6 (2 × C, *C*O of 2 diastereomers), 169.5, 169.6 (2 × C, *C*O of 2 diastereomers); HRMS (ES+): Exact mass calculated for $C_{13}H_{15}NO_3Cl$ $[M+H]^+$, 268.0740. Found 268.0731; m/z (ES+) 268.0 {[$(C_{13}H_{14}NO_3Cl)+H^+$], 12%]}, 219.1 (100%).

(4*S*)-4-Benzyl-3-[2-(phenylthio)propanoyl]oxazolidin-2-one 2

Benzenethiol (1.67 mL, 16.4 mmol) was added to a solution of freshly prepared sodium ethoxide [prepared from sodium (0.38 g, 16.4 mmol) in dry ethanol (40 mL) at 0 °C] while stirring under nitrogen. After stirring for 20 min, a solution of (4*S*)-4-benzyl-3-(2-chloropropanoyl)oxazolidin-2-one **1** (3.99 g, 14.9 mmol) in ethanol (150 mL) was added gradually to the reaction mixture over 15 min. Following stirring at room temperature for 2 h, the reaction was quenched by the addition of water (150 mL) and dichloromethane (150 mL). The combined organic layers were washed with aqueous sodium hydroxide (1 M, 2 × 150 mL), water (150 mL) and brine (150 mL), dried and concentrated under reduced pressure to give the crude sulfide as a clear oil. This was purified by column chromatography on silica gel using hexane-ethyl acetate as eluent (gradient elution 5-10 % ethyl acetate) to give the sulfide **2** (4.58 g, 90%) as a clear oil and an equimolar mixture of diastereomers; $[\alpha]_D^{20}$ +95.2 (*c* 0.5 in EtOH); ν_{max}/cm^{-1} (film) 3061 (CH), 2929 (CH), 1779 (CO oxazolidinone), 1697 (CO); δ_H (300 MHz, $CDCl_3$) 1.46 [1.5H, d, *J* 6.9, C(3)H_3 of 1 diastereomer], 1.49 [1.5H, d, *J* 6.9, C(3)H_3 of 1 diastereomer], 2.66 (0.5H, dd, A of ABM, J_{AB} 13.2, J_{AM} 9.9, C$H_A$$H_B$Ph of 1 diastereomer), 2.75 (0.5H, dd, A of ABM, J_{AB} 13.2, J_{AM} 9.6, C$H_A$$H_B$Ph of 1 diastereomer), 3.26-3.33 (1H, 2 overlapping dd, B of ABM, J_{AB} 13.2, J_{BM} 6.6, CH$_A$$H_B$Ph of 1 diastereomer and B of ABM, J_{AB} 13.2, J_{BM} 3.3, CH$_A$$H_B$Ph of 1 diastereomer), 4.00-4.25 (2H, m, CH_2O of 2 diastereomers), 4.49-4.61 (0.5H, m, C*H*N of 1 diastereomer), 4.64-4.77 (0.5H, m, C*H*N of 1 diastereomer), 5.15-5.23 [1H, 2 × overlapping q, *J* 6.9, 6.9, C(2)*H* of 2 diastereomers], 7.15-

7.39 (8H, m, Ar*H* of 2 diastereomers), 7.43-7.57 (2H, m, Ar*H* of 2 diastereomers); δ_C (150 MHz, $CDCl_3$) 16.7, 16.8 [2 × CH_3, *C*(3)H_3 of 2 diastereomers], 37.7, 37.9 (2 × CH_2, *C*H_2Ph of 2 diastereomers), 42.3, 42.6, 55.3, 55.8 [4 × CH, *C*(2)H & *C*HN of 2 diastereomers], 66.1, 66.2 (2 × CH_2, O*C*H_2 of 2 diastereomers), 127.38, 127.41, 128.7, 128.8, 128.92, 128.94, 128.98, 129.02, 129.4 (9 × CH, 9 × aromatic *C*H), 131.5, 131.6 (2 × C, 2 × aromatic *C*), 134.76, 134.79 (2 × CH, 2 × aromatic *C*H), 135.2 (C, aromatic *C*), 152.9, 153.0 (2 × C, *C*O of 2 diastereomers), 172.1, 172.2 (2 × C, *C*O of 2 diastereomers); HRMS (ES+): Exact mass calculated for $C_{19}H_{20}NO_3S$ $[M+H]^+$, 342.1164. Found 342.1148; m/z (ES+) 342.0 {[($C_{19}H_{20}NO_3S$)+H^+], 100%]}, 104.9 (28%).

(4*S*)-4-Benzyl-3-[2-(benzylthio)propanoyl]oxazolidin-2-one 3

Sodium hydride (0.50 g of a 60% dispersion in mineral oil, 12.5 mmol) was placed in a three-necked round bottom flask under a flow of nitrogen. Following washing with hexane (3 × 10 mL), dry *N*,*N*-dimethylformamide (60 mL) was added and the resulting suspension was stirred for 10 min. The reaction mixture was cooled to 0 °C and benzyl thiol (1.47 mL, 12.5 mmol) was added slowly *via* syringe. After stirring for 20 min, a solution of (4*S*)-4-benzyl-3-(2-chloropropanoyl)oxazolidin-2-one (3.14 g, 11.7 mmol) in dry *N*,*N*-dimethylformamide (20 mL) was added. On completion of the addition, the ice bath was removed and the reaction mixture stirred at room temperature for 4 h. The reaction was quenched by the addition of water (60 mL) and dichloromethane (60 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane (2 × 60 mL), and the combined organic layers were washed with sodium hydroxide (1 M, 60 mL), water (2 × 60 mL), hydrochloric acid (2 M, 2 × 60 mL) and brine (60 mL), dried, filtered and concentrated at reduced pressure to give the crude sulfide **3** as a pale yellow oil and a 1:1.24 mixture of diastereomers. This was purified by column chromatography on silica gel using hexane-ethyl acetate as eluent (gradient

elution 10-20 % ethyl acetate) to give the less polar minor diastereomer as a clear oil (1.42 g, 34%) and the more polar major diastereomer as a clear oil (1.75 g, 43%); Minor diasteromer: $[\alpha]_D^{20}$ +138.5 (*c* 0.04 in $CHCl_3$); ν_{max}/cm^{-1} (film) 1778 (CO oxazolidinone), 1694 (CO); δ_H (300 MHz, $CDCl_3$) 1.52 [3H, d, *J* 7.2, C(3)H_3], 2.71 (1H, dd, A of ABM, J_{AB} 13.5, J_{AM} 9.9, C$H_A$$H_B$Ph), 3.23 (1H, dd, B of ABM, J_{AB} 13.5, J_{AM} 3.3, CH$_A$$H_B$Ph), 3.81 (1H, A of AB system, *J* 13.5, one of SCH_2), 3.87 (1H, B of AB system, *J* 13.5, one of SCH_2), 3.97-4.12 (2H, m, CH_2O), 4.24-4.34 (1H, m, C*H*N), 4.83 [1H, q, *J* 7.2, C(2)*H*], 7.12-7.39 (10H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 17.2 [CH_3, *C*(3)H_3], 34.6 (CH_2, *C*H_2Ph), 37.9 (CH_2, S*C*H_2), 39.3, 55.6 [2 × CH, *C*(2)H & *C*HN], 66.1 (CH_2, O*C*H_2), 127.1, 127.4, 128.4, 129.0, 129.1, 129.4 (6 × CH, 6 × aromatic *C*H), 135.2, 137.9 (2 × C, 2 × aromatic *C*), 153.0 (C, *C*O), 172.4 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{20}H_{21}NO_3S^{23}Na$ $[M+Na]^+$, 378.1140. Found 378.1138; m/z (ES+) 356.2 {[($C_{20}H_{21}NO_3S$)+H^+], 100%]}, 213.2 (4%), 104.9 (12%).

Major diasteromer: $[\alpha]_D^{20}$ −27.4 (*c* 0.04 in $CHCl_3$); ν_{max}/cm^{-1} (film) 1777 (CO oxazolidinone), 1693 (CO); δ_H (300 MHz, $CDCl_3$) 1.50 [3H, d, *J* 6.9, C(3)H_3], 2.67 (1H, dd, A of ABM, J_{AB} 13.5, J_{AM} 9.9, C$H_A$$H_B$Ph), 3.21 (1H, dd, B of ABM, J_{AB} 13.5, J_{AM} 3.3, CH$_A$$H_B$Ph), 3.85 (1H, A of AB system, J_{AB} 12.6, one of SCH_2), 3.90 (1H, B of AB system, J_{AB} 12.6, one of SCH_2), 4.10-4.23 (2H, m, CH_2O), 4.64-4.75 (1H, m, C*H*N), 4.87 (1H, q, *J* 6.9, C(2)*H*), 7.18-7.39 (10H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 16.9 [CH_3, *C*(3)H_3], 34.3 (CH_2, *C*H_2Ph), 37.5 (CH_2, S*C*H_2), 39.2, 55.2 [CH, *C*(2)H & *C*HN], 66.0 (CH_2, O*C*H_2), 127.2, 127.4, 128.6, 129.0, 129.2, 129.5 (6 × CH, 6 × aromatic *C*H), 135.2, 137.5 (2 × C, 2 × aromatic *C*), 153.0 [C, *C*O], 172.0 [C, *C*O]; HRMS (ES+): Exact mass calculated for $C_{20}H_{21}NO_3S^{23}Na$ $[M+Na]^+$, 378.1140. Found 378.1134; m/z (ES+) 356.2 {[($C_{20}H_{21}NO_3S$)+H^+], 100%]}.

For subsequent reactions the 2 diastereomers were combined (ratio of diastereomers 1:1.24) and the specific rotation of the mixture was recorded; $[\alpha]_D^{20}$ +34.6 (*c* 0.5, $CHCl_3$) (of mixture of diasteromers).

(*S*)-4-Benzyl-3-[(*E*)-3-chloro-2-(phenylthio)acryloyl]oxazolidin-2-one 4 & (*S*)-4-Benzyl-3-[(*Z*)-3-chloro-2-(phenylthio)acryloyl]oxazolidin-2-one 5

Unrecrystallised *N*-chlorosuccinimide (4.00 g, 29.4 mmol) was added in one portion to a solution of the sulfide (4*S*)-3-[2-(phenylthio)propanoyl]-4-benzyloxazolidin-2-one **2** (4.56 g, 13.4 mmol) in toluene (80 mL). The flask was immediately immersed in an oil bath at 130 °C and heating was maintained for 15 min with stirring. The reaction mixture was cooled to 0 °C and the succinimide by-product was removed by filtration. The solvent was evaporated at reduced pressure to give the crude product as a clear oil, ratio of **4**:**5** 1:1.05. Following purification by column chromatography on silica gel using hexane-ethyl acetate as eluent (gradient elution 5-40% ethyl acetate), **4** (1.42 g, 29%) was isolated as a low melting white solid; $[\alpha]_D^{20}$ +11.1 (*c* 2.5 in EtOH); ν_{max}/cm^{-1} (film) 3063 (CH), 2922 (CH), 1790 (CO oxazolidinone), 1688 (CO); δ_H (300 MHz, $CDCl_3$) (the spectrum of this compound is very poorly resolved in the oxazolidinone region of δ_H 2-5) 2.59-2.82 (1H, br m, C$H_A$$H_B$Ph), 3.20-3.39 (1H, br m, C$H_A$$H_B$Ph), 4.07-4.20 (2H, m, C$H_2$O), 4.49-4.73 (1H, br m, C*H*N), 6.73 [1H, s, Cl*H*C(3)=], 7.13-7.64 (10H, m, Ar*H*); δ_C (125 MHz, $CDCl_3$) 37.5 (CH_2, *C*H_2Ph), 55.0 (CH, *C*HN), 66.4 (CH_2, *C*H_2O), 124.8 (C, aromatic *C*), 127.4, 128.1, 128.99, 129.01, 129.1, 129.26, 129.29, 129.4, 129.8, 130.9, 131.2, 134.9 [3 × CH, aromatic *C*H or ClH*C*(3)=], 151.6 (C, *C*O), 161.8, 163.3 (2 × C, *C*O); HRMS (ES+): Exact mass calculated for $C_{19}H_{17}NO_3SCl$ $[M+H]^+$, 374.0618. Found 374.0604; 374.0 ($[C_{19}H_{16}NO_3SCl$ $+H)^+$, 28%).

5 (1.11 g, 22%) was isolated as a white solid, mp 97-99 °C; $[\alpha]_D^{20}$ +5.5 (*c* 2.5 in DCM); (Found C, 61.21; H, 4.70; N, 3.65; S, 8.54; Cl, 9.70. $C_{19}H_{16}ClNO_3S$ requires C, 61.04; H, 4.31; N, 3.75; S, 8.58; Cl, 9.48); ν_{max}/cm^{-1} (KBr) 2919 (CH), 1788 (CO oxazolidinone), 1678 (CO); δ_H (300 MHz, $CDCl_3$) 2.26 (1H, dd, *J* 13.4, 10.0, C*H*$_A$H$_B$Ph), 3.00 (1H, overlapping dd, *J* 13.5, 3.6, CH$_A$*H*$_B$Ph), 3.84-3.93 (1H, m, one of C*H*$_2$O), 3.98 (1H, dd, *J* 9.0, 3.9, one of C*H*$_2$O), 4.21-4.30 (1H, br m, C*H*N), 6.80 [1H, s, Cl*H*C(3)=], 7.04-7.11 (2H, m, Ar*H*), 7.22-7.37 (6H, m, Ar*H*), 7.44-7.52 (2H, m, Ar*H*); δ_C (125 MHz, $CDCl_3$) 37.1 (CH_2, *C*H$_2$Ph), 55.5 (CH, *C*HN), 66.6 (CH_2, O*C*H$_2$), 126.4, 127.4, 128.5, 129.0, 129.3, 129.4 [6 × CH, aromatic *C*H or ClH*C*(3)=], 131.2 [C, aromatic *C* or *C*(2)S], 132.5 [CH, aromatic *C*H or ClH*C*(3)=], 134.7, 134.8 [2 × C, aromatic *C* or *C*(2)S], 151.8 (C, *C*O), 164.1 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{19}H_{17}NO_3SCl$ $[M+H]^+$, 374.0618. Found 374.0602; 374.0 ($[C_{19}H_{16}NO_3SCl+H)^+$, 50%).

5-(Benzylthio)-3-(1-chloro-3-phenylpropan-2-yl)-5-(dichloromethyl)oxazolidine-2,4-dione-one 7 & (*S*)-4-Benzyl-3-[(*E*)-2-(benzylthio)-3-chloroacryloyl]oxazolidin-2-one 6

Unrecrystallised *N*-chlorosuccinimide (2.63 g, 19.3 mmol) was added in one portion to a solution of the sulfide (4*S*)-4-benzyl-3-[2-(benzylthio)propanoyl]oxazolidin-2-one **3** (3.12 g, 8.8 mmol) in toluene (60 mL). The flask was immediately immersed in an oil bath at 130 °C and heating was maintained for 30 min with stirring. The reaction mixture was cooled to 0 °C and the succinimide by-product was removed by filtration. The solvent was evaporated at reduced pressure to give the crude product as an orange oil, ratio of **7:6** 0.43:1. Following purification by column chromatography on silica gel using hexane-ethyl acetate as eluent (gradient elution 5-40% ethyl acetate), **7** was isolated as a white solid (0.45 g, 9%); (Found C, 52.48; H, 4.03; N, 3.00. $C_{20}H_{18}Cl_3NO_3S$ requires C, 52.36; H, 3.95; N, 3.05%); ν_{max}/cm^{-1} (KBr) 3028 (CH), 2924 (CH), 1827 (CO), 1754 (CO); δ_H (300 MHz, $CDCl_3$) 3.19 (1H, dd, A

of ABX, J_{AB} 14.3, J_{AX} 6.9, one of NCHCH_2), 3.27 (1H, dd, B of ABX, J_{AB} 14.3, J_{BX} 9.6, one of NCHCH_2), 3.73 (1H, dd, A of ABX, J_{AB} 11.9, J_{AX} 4.5, one of CH_2Cl), 3.78 (1H, d, A of AB system, J_{AB} 11.4, one of SCH_2), 3.83 (1H, d, B of AB system, J_{AB} 11.4, one of SCH_2), 4.08 (1H, dd, B of ABX, J_{AB} 11.9, J_{BX} 10.2, one of CH_2Cl), 4.64-4.75 (1H, br m, C*H*N), 5.82 (1H, s, C*H*Cl_2), 7.14-7.36 (10H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 34.6, 35.5 (2 × CH_2, NCH*C*H_2 & S*C*H_2), 42.4 (CH_2, *C*H_2Cl), 56.9 (CH, *C*HN), 70.6 (CH, *C*HCl_2), 92.9 [C, *C*(5)], 127.6, 128.2, 128.9, 129.0, 129.1, 129.3 (6 × CH, 6 × aromatic *C*H), 133.9, 135.0 (2 × C, 2 × aromatic *C*), 151.9 (C, *C*O), 167.8 (C, *C*O).

The structure of **7** was determined by single crystal X-ray diffraction on a crystalline sample of **7** recrystallised from ethanol. Crystals of **7** are orthorhombic, space group $P\ 2_12_12_1$, formula $C_{20}H_{18}Cl_3NO_3S$, M = 458.76, a = 9.4675(9) Å, b = 10.1086(9) Å, c = 21.340(2) Å, α = 90.00 °, β = 90.00 °, γ = 90.00 °, U = 2042.3(3) $Å^3$, F(000) = 944, μ(Mo-Kα) = 0.573 mm^{-1}, $R(F_o)$ = 0.0574, for 4406 observed reflections with I>2σ(I), $wR_2(F^2)$ = 0.1525 for all 5951 unique reflections. Data in the θ range 1.91-30.00 ° were collected at 100 K on a Bruker Apex II Duo diffractometer using Mo-Kα radiation, λ = 0.71073 Å, and corrected for Lorentz and polarisation effects. The structure was solved by direct methods and refined by full-matrix least-squares using all F^2 data. The hydrogen atoms were placed in calculated positions and allowed to ride on the parent atom.

6 (1.41 g, 41%) was isolated as a white solid, mp 97-99 °C; $[\alpha]_D^{20}$ +63.2 (0.5, $CHCl_3$); (Found C, 61.61; H, 4.58; N, 3.62; S, 8.27; Cl, 9.38. $C_{20}H_{18}ClNO_3S$ requires C, 61.93; H, 4.68; N, 3.61; S, 8.27; Cl, 9.14%); ν_{max}/cm^{-1} (KBr) 3074 (CH), 2917 (CH), 1773 (CO oxazolidinone), 1674 (CO); δ_H (300 MHz, $CDCl_3$) (The spectrum of this compound was very poorly resolved in the region of δ_H 3-5) 2.77 (1H, dd, A of ABX, J_{AB} 13.5, J_{AX} 9.9, C$H_A$$H_B$Ph), 3.32-3.45 (1H, br m, C$H_A$$H_B$Ph), 3.93 (2H, s, SC$H_2$), 4.14-4.22 (2H, br m, CH_2O), 4.53-4.73 (1H, br m,

C*H*N), 6.33 [1H, s, Cl*H*C(3)=], 7.20-7.41 (10H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 37.7, 39.0 (2 × CH_2, S*C*H_2 & *C*H_2Ph), 55.0 (CH, *C*HN), 66.4 (CH_2, O*C*H_2), 125.5, 127.5, 128.5, [3 × CH, aromatic *C*H or ClH*C*(3)=], 128.6 [C, aromatic *C* or *C*(2)S], 129.1, 129.3, 129.4, 129.5 [4 × CH, aromatic *C*H or ClH*C*(3)=], 135.0, 137.0 [2 × C, aromatic *C* or *C*(2)S], 151.6 (C, *C*O), 164.1 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{20}H_{19}NO_3SCl$ $[M+H]^+$, 388.0774. Found 388.0789; 388 ($[M+H)^+$, 54%).

An X-ray crystal structure of the sulfoxide derivative **8** was obtained, which confirmed the relative stereochemistry as *E*. The relative stereochemistry of **6** was assigned by analogy.

(*S*)-4-Benzyl-3-[(*E*)-3-chloro-2-(*S*s/*R*s)-(benzenesulfinyl)acryloyl]oxazolidin-2-one 15

A solution of Oxone® (0.85 g, 1.4 mmol) in water (5 mL) was added to a stirring solution of (*S*)-4-benzyl-3-[(*E*)-3-chloro-2-(phenylthio)acryloyl]oxazolidin-2-one **4** (0.26 g, 0.7 mmol) in acetone (20 mL) at room temperature. A colourless precipitate formed immediately. The reaction mixture was stirred for 40 h. Water (20 mL) was added and the aqueous solution was extracted with dichloromethane (3 × 20 mL). The combined extracts were washed with water (2 × 20 mL) and brine (20 mL), dried, filtered and concentrated at reduced pressure to give the crude sulfoxides **15a** and **15b** as a white sticky solid and a 1 : 0.91 mixture of diastereomers. Following purification by column chromatography on silica gel using dichloromethane-methanol as eluent (gradient elution 0-0.5% methanol), the less polar minor diastereomer **15b** was isolated as a low melting white solid (0.13 g, 48%); ν_{max}/cm^{-1} (film) 3066 (CH), 2919 (CH), 1795 (CO oxazolidinone), 1687 (CO), 1085 (SO); δ_H (300 MHz, $CDCl_3$) 2.71 (1H, dd, A of ABX, J_{AB} 13.5, J_{AX} 10.5, C$H_A$$H_B$Ph), 3.32-3.47 (1H, br m, C$H_A$$H_B$Ph), 4.15-4.27 (2H, m, C$H_2$O), 4.64-4.85 (1H, br m, C*H*N), 7.15-7.42 (5H, m, Ar*H*),

7.50-7.77 [4H, m, Ar*H* & Cl*H*C(3)=], 7.92 (2H, d, *J* 7.5, Ar*H*); m/z (ES+) 392.0 {[($C_{19}H_{16}NO_4S^{37}Cl$)+H^+], 16%}, 390.0 {[($C_{19}H_{16}NO_4S^{35}Cl$)+H^+], 36%}.

A second fraction containing the more polar major diastereomer **15a** was also isolated (0.06 g, 27%) as a white solid; ν_{max}/cm^{-1} (KBr) 3061 (CH), 2923 (CH), 1789 (CO oxazolidinone), 1685 (CO), 1081 (SO); δ_H (300 MHz, $CDCl_3$) 2.79 (1H, dd, *J* 13.5, 9.3, CH_AH$_B$Ph), 3.41 (1H, dd, *J* 13.5, 3.6, CH$_A$$H_B$Ph), 4.22 (1H, dd, *J* 9.0, 3.0, one of CH_2O), 4.34 (1H, dd, *J* 9.0, 8.1, one of CH_2O), 4.69-4.86 (1H, br m, C*H*N), 7.02-7.99 [11H, m, Ar*H* & Cl*H*C(3)=]; m/z (ES+) 392.0 {[($C_{19}H_{16}NO_4S^{37}Cl$)+H^+], 12%}, 390.0 {[($C_{19}H_{16}NO_4S^{35}Cl$)+H^+], 26%}.

The ^{13}C NMR spectrum was recorded on a 3:1 mixture of **15a** and **15b**: δ_C ($CDCl_3$, 67.8 MHz) 37.3, 37.8* (*C*H$_2$Ph), 55.1*, 55.6 (*C*HN), 66.5*, 66.8 (*C*H$_2$O), 125.7, 126.0, 127.1, 127.9, 129.3, 129.4, 132.5, 132.6, 134.3, 134.7, 139.2, 151.0 [aromatic CH, aromatic C, *C*(2)S and ClH*C*(3)=].

*Minor diastereomer

(*S*)-4-Benzyl-3-[(*Z*)-3-chloro-2-(*Ss*/*Rs*)-(benzenesulfinyl)acryloyl]oxazolidin-2-one 16 & (*S*)-4-benzyl-3-[(*Z*)-3-chloro-2-(benzenesulfonyl)acryloyl]oxazolidin-2-one 17

A solution of *m*CPBA (0.08 g of 77% pure material, 0.4 mmol) in dichloromethane (4 mL) was added to a stirring solution of (*S*)-4-benzyl-3-[(*Z*)-3-chloro-2-(phenylthio)acryloyl]oxazolidin-2-one **5** (0.12 g, 0.3 mmol) in dichloromethane (4 mL) at room temperature. Following stirring at room temperature for 1 h, the reaction was quenched by addition of saturated sodium bicarbonate (10 mL). The layers were separated and the aqueous layer was washed with dichloromethane (2 × 10 mL). The combined organic layers were washed with water (2 × 10 mL) and brine (10 mL), dried and concentrated to give the product as a white sticky solid and a 1:0.68:0.53 mixture of **16a**:**16b**:**17** sulfone:sulfoxide diastereomers. Following purification by column chromatography on silica gel using hexane-

ethyl acetate as eluent (gradient elution 10-20% ethyl acetate), the less polar minor sulfoxide diastereomer **16b** was isolated as a low melting white solid (0.006 g, 5%); δ_H (300 MHz, $CDCl_3$) 2.81 (1H, dd, A of ABX, J_{AB} 13.8, J_{AX} 10.5, C*H*$_A$H$_B$Ph), 3.53 (1H, dd, B of ABX, J_{AB} 13.8, J_{BX} 3.6, C*H*$_A$H$_B$Ph), 4.09-4.16 (1H, m, C*H*$_A$H$_B$OH), 4.19 (1H, dd, B of ABX, J_{AB} 9.0, J_{BX} 3.3, CH$_A$*H*$_B$OH), 4.57-4.68 (1H, br m, C*H*N), 6.72 [1H, s, Cl*H*C(3)=], 7.19-7.41 (5H, m, Ar*H*), 7.48-7.63 (3H, m, Ar*H*), 7.80-7.92 (2H, m, Ar*H*); m/z (ES+) 392.1 {[($C_{19}H_{16}NO_4S^{37}Cl$)+H^+], 42%}, 390.1 {[($C_{19}H_{16}NO_4S^{35}Cl$)+H^+], 100%}.

A second fraction containing a mixture of the less polar sulfoxide diastereomer **16b** and the sulfone **17** in a ratio of 1:4.7 respectively was isolated (0.009 g, 7%) as a white solid. The sulfone **17** was seen at δ_H (300 MHz, $CDCl_3$) 2.89 (1H, dd, A of ABX, J_{AB} 13.5, J_{AX} 9.9, C*H*$_A$H$_B$Ph), 3.45 (1H, dd, B of ABX, J_{AB} 13.5, J_{BX} 3.6, C*H*$_A$H$_B$Ph), 4.27 (1H, dd, A of ABX, J_{AB} 9.0, J_{AX} 3.3, C*H*$_A$H$_B$OH), 4.35 (1H, dd, B of ABX, J_{AB} 9.0, J_{BX} 7.8, CH$_A$*H*$_B$OH), 4.72-4.84 (1H, br m, C*H*N), 6.87 [1H, s, Cl*H*C(3)=], 7.19-7.42 (5H, m, Ar*H*), 7.49-7.75 (3H, m, Ar*H*), 8.03-8.13 (2H, m, Ar*H*); m/z (ES+) 408.1 {[($C_{19}H_{16}NO_5S^{37}Cl$)+H^+], 26%}, 406.1 {[($C_{19}H_{16}NO_5S^{35}Cl$)+H^+], 58%}, 392.1 {[($C_{19}H_{16}NO_4S^{37}Cl$)+H^+], 22%}, 390.1 {[($C_{19}H_{16}NO_4S^{35}Cl$)+H^+], 54%}.

A fraction containing the more polar major sulfoxide diastereomer **16a** was also isolated as a white solid (0.009 g, 7%); δ_H (300 MHz, $CDCl_3$) 2.72 (1H, dd, A of ABX, J_{AB} 13.5, J_{AX} 9.9, C*H*$_A$H$_B$Ph), 3.25 (1H, dd, B of ABX, J_{AB} 13.5, J_{BX} 3.6, C*H*$_A$H$_B$Ph), 4.19 (1H, dd, A of ABX, J_{AB} 9.0, J_{AX} 3.0, C*H*$_A$H$_B$OH), 4.33 (1H, overlapping dd, B of ABX, J_{AB} 9.0, J_{BX} 8.1, CH$_A$*H*$_B$OH), 4.67-4.79 (1H, br m, C*H*N), 6.75 [1H, s, Cl*H*C(3)=], 7.12-7.40 (5H, m, Ar*H*), 7.48-7.63 (3H, m, Ar*H*), 7.80-7.91 (2H, m, Ar*H*); m/z (ES+) 392.1 {[($C_{19}H_{16}NO_4S^{37}Cl$)+H^+], 42%}, 390.1 {[($C_{19}H_{16}NO_4S^{35}Cl$)+H^+], 100%}.

The ^{13}C NMR spectrum was recorded on a 1.65:1:1.19 mixture of **16a : 16b : 17**: δ_C ($CDCl_3$, 67.8 MHz) 37.7, 37.8*, 38.2^i (3 × CH_2, *C*H$_2$Ph), 55.66^i, 55.72, 55.8* (3 × CH, *C*HN), 66.9*,

67.16, 67.20[i] (3 × CH_2, *C*H_2O), 126.2, 126.3, 126.4, 126.8, 127.0, 127.9, 129.2, 129.36, 129.41, 129.6, 129.7, 129.8, 132.5, 133.1, 134.7 [15 × CH, aromatic *C*H and ClH*C*(3)=], 135.5, 140.3, 142.0, 142.9, 143.1, 145.6, 145.7, 152.9, 153.1, 160.6[i], 160.7, 160.9 [12 × C, *C*O, aromatic C and *C*(2)S]; HRMS (ES+): Exact mass calculated for $C_{19}H_{17}NO_5SCl$ (**17**) $[M+H]^+$, 406.0516. Found 406.0510; Exact mass calculated for $C_{19}H_{17}NO_4SCl$ (**16a & 16b**) $[M+H]^+$, 390.0567. Found 390.0558; 406.1 (8%), 390.1 (100%).

*Minor diastereomer

[i]Major diasteromer

(*S*)-4-Benzyl-3-[(*E*)-2-(*S*s/*R*s)-(benzylsulfinyl)-3-chloroacryloyl]oxazolidin-2-one 8 & (*S*)-4-Benzyl-3-[(*E*)-2-(benzylsulfonyl)-3-chloroacryloyl]oxazolidin-2-one 18

A solution of Oxone® (0.60 g, 1.0 mmol) in water (5 mL) was added to a stirring solution of (*S*)-4-benzyl-3-[(*E*)-2-(benzylthio)-3-chloroacryloyl]oxazolidin-2-one **6** (0.19 g, 0.5 mmol) in acetone (20 mL) at room temperature. A colourless precipitate formed immediately. The reaction mixture was stirred for 16 h. Water (20 mL) was added and the aqueous solution was extracted with dichloromethane (3 × 20 mL). The combined extracts were washed with water (2 × 20 mL) and brine (20 mL), dried, filtered and concentrated at reduced pressure to give the crude product as a white solid and a mixture of **8a**, **8b*** and **18** in a ratio of 1:0.03:0.7 respectively (by ^{1}H NMR spectroscopy). Following purification by column chromatography on silica gel using hexane-ethyl acetate as eluent (gradient elution 10-20% ethyl acetate), **18** was isolated as a white solid (0.03 g, 16%), mp 162-164 °C; (Found C, 56.94; H, 4.34; N, 3.25; S, 7.84; Cl, 8.30. $C_{20}H_{18}ClNO_5S$ requires C, 57.21; H, 4.32; N, 3.34; S, 7.64; Cl, 8.44%); ν_{max}/cm^{-1} (KBr) 3072 (CH), 2921 (CH), 1784 (CO), 1671 (CO), 1390 (asymmetric SO_2 stretch), 1116 (symmetric SO_2 stretch); δ_H (300 MHz, $CDCl_3$) (This spectrum was very poorly resolved) 2.72-2.99 (1H, br m, C$H_A$$H_B$Ph), 3.36-3.59 (1H, br m, C$H_A$$H_B$Ph), 4.18-4.65

(4H, br m, SCH_2 & CH_2OH), 4.73-4.90 (1H, br m, C*H*N), 6.70 [0.42H, s, Cl*H*C(3)=], 6.78 [0.58H, s, Cl*H*C(3)=], 7.19-7.58 (10H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 37.2/37.9* (2 × CH_2, *C*H_2Ph), 55.3*/55.5 (2 × CH, *C*HN), 61.6*/61.8, 66.6 (major and minor) (3 × CH_2, O*C*H_2 & S*C*H_2), 127.6, 128.8*, 129.0, 129.2, 129.4, 131.3 (6 × CH, 6 × aromatic *C*H), 134.6, 135.3, 135.8 [3 × C, 2 × aromatic *C* & *C*(2)S], 136.6/137.5* [2 × CH, ClH*C*(3)=], 151.1 (major and minor) (C, *C*O), 160.1 (major and minor) (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{20}H_{19}NO_5S^{35}Cl$ $[M+H]^+$ 420.0672. Found 420.0655; m/z (ES+) 422.2 {[($C_{20}H_{18}NO_5S^{37}Cl$)+H^+], 42%}, 420.0 {[($C_{20}H_{18}NO_5S^{35}Cl$)+H^+], 100%}.

*Signals for major diastereomer

The more polar fraction contained **8a** (0.03 g, 17%) which was isolated as a white solid, mp 133-135 °C; $[\alpha]_D^{20}$ –10.8 (0.5, $CHCl_3$); (Found C, 59.18; H, 4.48; N, 3.38; S, 7.84; Cl, 8.80. $C_{20}H_{18}ClNO_4S$ requires C, 59.48; H, 4.49; N, 3.47; S, 7.94; Cl, 8.78%); ν_{max}/cm^{-1} (KBr) 3060 (CH), 2917 (CH), 1787 (CO oxazolidinone), 1667 (CO), 1061 (SO); δ_H (300 MHz, $CDCl_3$) 2.80 (1H, dd, A of ABX, J_{AB} 13.5, J_{AX} 9.9, C$H_A$$H_B$Ph), 3.41 (1H, dd, B of ABX, J_{AB} 13.5, J_{AX} 3.6, C$H_A$$H_B$Ph), 4.18-4.46 (4H, m, S*C*H_2 & *C*H_2O), 4.66-4.81 (1H, m, C*H*N), 6.33 [1H, s, Cl*H*C(3)=], 7.18-7.50 (10H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 37.9 (CH_2, *C*H_2Ph), 55.3 (CH, *C*HN), 60.4, 66.7 (2 × CH_2, O*C*H_2 & S*C*H_2), 126.5, 127.6 (2 × CH, aromatic *C*H), 128.2 (C, aromatic *C* or S*C*=), 128.7, 129.1, 129.4, 131.0 [4 × CH (for 5 carbons), aromatic *C*H & ClH*C*(3)=], 134.7, 139.1 (2 × C, aromatic *C* or S*C*=), 151.6 (C, CO), 160.7 (C, CO); HRMS (ES+): Exact mass calculated for $C_{20}H_{19}NO_4S^{35}Cl$ $[M+H]^+$ 404.0723. Found 404.0715; m/z (ES+) 406.2 {[($C_{20}H_{18}NO_4S^{37}Cl$)+H^+], 40%}, 404.2 {[($C_{20}H_{18}NO_4S^{35}Cl$)+H^+], 100%}.

The stereochemistry of **8a** was determined by single crystal X-ray diffraction on a crystalline sample of **8a** recrystallised from dichloromethane and hexane.

Crystals of **8a** are monoclinic, space group *P* 2_1, formula $C_{20}H_{18}ClNO_4S$, M = 403.86, a = 6.3053(7) Å, b = 23.418(4) Å, c = 12.9820(13) Å, α = 90.00 °, β = 90.715(10) °, γ = 90.00 °, U = 1916.8(4) $Å^3$, F(000) = 840, μ(Cu-Kα) = 3.007 mm^{-1}, R(F_o) = 0.1125, for 4041 observed reflections with I>2σ(I), wR_2(F^2) = 0.3225 for all 4887 unique reflections. Data in the θ range 3.40-67.42 ° were collected at 293 K on an Oxford Gemini R Ultra diffractometer using Cu-Kα graphite monochromated radiation, λ = 1.54184 Å, and corrected for Lorentz and polarization effects. The structure was solved by direct methods and refined by full-matrix least-squares using all F^2 data. The hydrogen atoms were placed in calculated positions and allowed to ride on the parent atom.

*Characteristic signals for **8b** were evident in the ^{1}H NMR of the crude product from the *m*CPBA reaction at δ_H (300 MHz, $CDCl_3$) 3.56 (1H, dd, *J* 13.5, 3.3, one of C*H*$_2$Ph), 4.79-4.87 (1H, m, CHN), 6.36 [1H, s, Cl*H*C(3)=].

Acknowledgements

IRCSET and University College Cork are gratefully acknowledged for funding of this work. We thank Oxford diffraction for data collection and structural analysis of compound **8a**.

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