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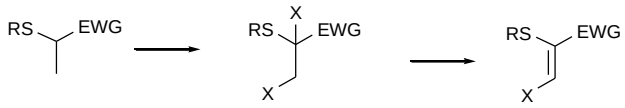
Graphical Abstract



EWG=Ester, Nitrile, Amide,

X=Cl, Br

Investigation of the Reaction of α-Thioamides, -esters and –nitriles with *N*-halosuccinimides

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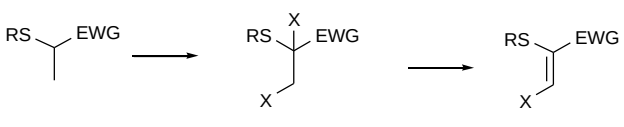
Abstract

Investigation of the reaction of α-thioamides, -esters and -nitriles with NBS and NCS is described. The scope of this stereoselective oxidative transformation to the β-haloacrylamides, -acrylates and –acrylonitriles has been determined. A mechanistic rationale to explain the observed differences in reactivity between the amide, ester and nitrile series is proposed.

Introduction

We have recently reported[1] the highly efficient and stereoselective transformation of α-thioamides to the corresponding α-thio-β-chloroacrylamide derivatives on treatment with NCS. As the highly functionalized acrylamides resulting from this transformation are potentially very useful synthetic intermediates, we wished to explore the scope of this transformation and, in particular, to establish if similar reactivity could be achieved with the analogous esters and nitriles, or by using thioamides with additional functional groups. In addition, it was decided to examine if replacement of NCS by NBS was possible leading to formation of the analogous bromides.



EWG=Ester, Nitrile, Amide,
X=Cl, Br

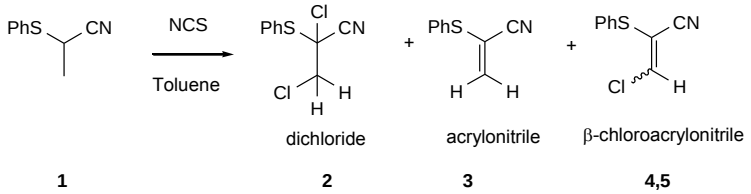
Results and Discussion

Nitrile Derivatives

The reaction of the α-thiopropionitrile[2,3] **1** with NCS was examined in detail (Table 1), with optimum conditions for the formation of the dichloride **2** determined as 1.95 equivalents of NCS in toluene at 140 °C for 18 h. In contrast to the amide series investigated earlier,[1] elimination from the dichloride **2** to the β–chloroacrylonitriles **4** & **5** did not occur under these conditions. It was previously shown that treatment of the analogous dichloride intermediates, formed during the reaction of α-thioamides with NCS, with $ZnCl_2$ gave the corresponding β-chloroacrylamides.[1] The decomposition of the dichloride **2** was thus attempted using 3 equivalents of $ZnCl_2$ in DCM under reflux conditions. After heating for 18 hours, the reaction was worked up to give a mixture of the *Z* and *E* β-chloroacrylonitriles **4** & **5** in a ratio of 6:1. Following chromatographic purification, a mixture of the *E* and *Z* β-chloroacrylonitriles was obtained as a yellow oil in the same ratio.

Thus, the methodology for the transformation of the amides to the corresponding β-chloroacrylamides is also applicable to the transformation of the α-thionitrile to the corresponding *E* and *Z* β-chloroacrylonitriles although in contrast to the amide series, use of $ZnCl_2$ is required to effect the final elimination in the nitrile series. In general, the transformation of the nitriles was found to be less robust than that of the amides with the outcome very sensitive to minor changes in the reaction conditions.

Table 1: Reaction of NCS with **1**



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

Eq. NCS	Oil Bath Temp. (°C)	Time (h)	% 2†	%3†	% 4,5†
2.1	130	18	20	80	-

1.95	130	18	40	60	-
2.1	130	48	66	33	<5
2.1	130	48	-	>90	-
2.1	160‡	18	Trace	Trace	-
1.95	140	18	73	9	18§
After $ZnCl_2$ decomposition			5	10	85

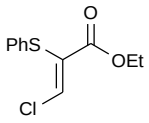
† As determined by ^{1}H NMR spectroscopy of the crude reaction product.

‡ This reaction was conducted in xylene, complex mixture of unidentified compounds formed.

§ Two signals were observed corresponding to the *E* and *Z* β-chloroacrylonitriles **4** & **5**. In the crude reaction mixture while **4** & **5** were present in limited amounts, the ratio of *Z*:*E* was 1:1. After treating with $ZnCl_2$, the ratio had changed to 6:1.

Extension to the Ester derivatives

The reaction of α-thioesters with NCS was investigated next to determine if they could be transformed to the β-chloroacrylates. While α-chlorosulfides of esters have been employed in other work,[4] to the best of our knowledge, only one previous report of α-sulfenyl-β-chloroacrylates has appeared in the literature. A 1985 patent by Viehe *et al.*[5] mentions the ethyl β-chloroacrylate **6b**. In the patent, the use of α-thio-β-halo-α,β-unsaturated esters and amides and β-haloacrylonitriles for reaction with nucleophiles is reported, although no experimental details are provided. In 1998, Hoffman *et al*[6] reported the preparation of *E* and *Z* β-fluoro-α-aminoacrylate derivatives **7,8** by condensation of methyl carbamate and the β-fluorinated α-oxo ester **9.**



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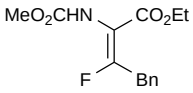

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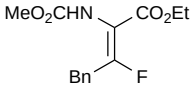

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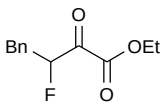
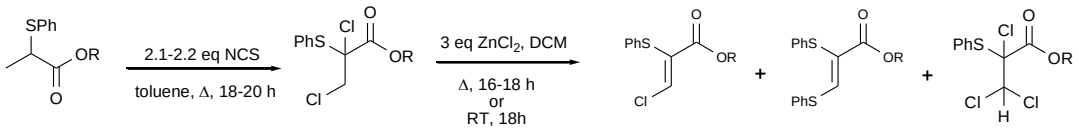


9

The esters **10a** & **10b**[4] were treated with 2.1-2.2 equivalents of NCS in toluene at 130 °C for 18 h to form the corresponding dichlorides **11a** & **11b** (Scheme 1).



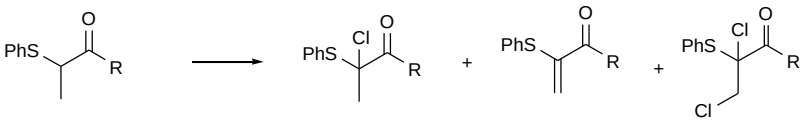
R=Me **10a** **11a** 87% 6a **70%** **12a** 13a
R=Et **10b** **11b** 85% 6b **71%** **Minor Products**

Scheme 1

Following our experience with the nitrile derivatives, it was envisaged that Lewis acid catalysed decomposition of the dichlorides **11a** & **11b** would produce the β-chloroacrylate **6a** & **6b**.

The α-chlorosulfide **14a** was also prepared by treatment of the α-thioester **10a** with NCS in toluene. To this end, 1.1 equivalents of NCS was added to a solution of the α-thioester **10a** in toluene at room temperature for 18 hours. The isolated product consisted of 70% α-chlorosulfide **14a** and 30% unreacted α-thioester **10a** (Table 2). Significantly, in the amide series under these conditions 50% of the α-chlorosulfide eliminated to form the acrylamide.[1] This indicates that the α-chlorosulfide derivative is less prone to elimination of HCl in the ester series than in the amide series. Furthermore, when 2.2 equivalents of NCS were used at room temperature for 18 hours with the α-thioamide, the acrylamide and the dichloride were formed.[1] What was found with the ester under these conditions, however, was that the α-thioester was converted to the α-chlorosulfide **14a** with just a trace of the acrylate seen by ^{1}H NMR spectroscopy (Table 2). Evidently, the α-chlorosulfide of the ester **14a** is more stable than that of the amide, with the loss of HCl from the α-chlorosulfide occurring much more readily when the amide functionality is present.

Table 2: Reaction of 10a & 10c with NCS



R=OCH$_3$ **10a** **14a** **15a** **11a**
R=NHTol **10c** **14c** **15c** **11c**

Experiment†	R	% 14a	% 15a	% 11a	% 14c	% 15c	% 11c
A	OCH_3	70‡	-	-			

B	OCH_3	>90	Trace	-			
A	NHTol				50	50	-
B	NHTol				-	33	66

†Experiment A= 1.1 eq.NCS, R.T., 18 h.

Experiment B= 2.2 eq.NCS, R.T., 18 h.

‡ The isolated product consisted of 70% **14a** and 30% **10a**.

Further evidence for the increased stability of the ester derivative was seen in the formation of the dichloride when **10a** is treated with 2.2 equivalents of NCS in toluene under reflux conditions (Scheme 1). In the amide series, the dichloride rapidly eliminates HCl under these conditions to give the β-chloroacrylamide.[1] Furthermore, extended storage of the dichloride **11a** was possible without apparent degradation.

The rationale for the increased ease of elimination in the amide series relative to the ester and nitrile series is presumably due to conformational properties; in the amides the intramolecular hydrogen bond holds the compound in a conformation in which loss of the chloride from the α-carbon is favored through captodative stabilization[7] of the resulting sulfur stabilized carbocation (Figure 1). In the ester derivative there is no restriction on the conformation and presumably the chlorosulfide adopts a different conformation from which the loss of chloride is less favoured. Another possible contributor to this is that the increased electron withdrawing effect of the ester compared to the amide destabilises a carbonium ion at the α-carbon therefore stabilising the chlorosulfide and dichloride.

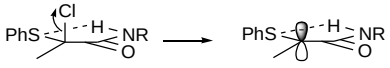


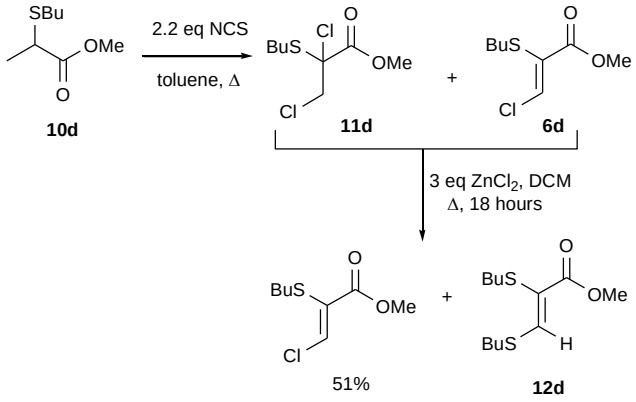
Figure 1

The decomposition of **11a** & **11b** to the corresponding β-chloroacrylates **6a** & **6b** was then achieved by reaction with 3 equivalents of $ZnCl_2$ in dichloromethane under reflux for 18 h (Scheme 1).

The formation of **6a** & **6b** was repeated on a number of occasions in up to a 24 mmol scale, with the *Z* isomer of the β-chloroacrylates formed exclusively in each instance. Also, the dichlorides can be carried forward with or without purification by chromatography, with no effect on the isolated yield of **6a** & **6b**.

Treatment of Methyl 2-(alkylthio)propanoates with NCS

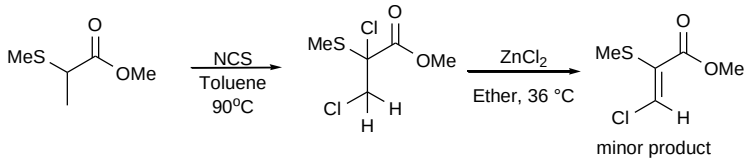
Treatment of the ester **10d** with the conditions outlined above for **10a** & **10b** resulted in a 1:2 mixture of the dichloride **11d** and the β-chloroacrylate **6d**. This was the first time that the β-chloroacrylate had formed to a substantial degree without the need for Lewis acid catalysed decomposition of the dichloride. Treatment of the crude reaction product with 3 equivalents of $ZnCl_2$ with respect to the remaining dichloride gave the β-chloroacrylate in 51% yield following chromographic purification. A trace amount of the bis-sulfide **12d** was also observed. As with the phenylthio derivatives of the β-chloroacrylates, no evidence for a second isomer of the β-chloroacrylate was observed (Scheme 2).



Scheme 2

The preparation of the methanethio-substituted β-chloroacrylate **6e** has also been attempted. When the α-thioester **10e**[8] was reacted with NCS (1.95 equivalents) in toluene at 90 °C, the dichloride **11e** was isolated as a colourless oil (Scheme 3). This compound was identified by the presence of a characteristic AB quartet at δ_H 4.85-5.05 with a coupling constant of 13 Hz in the ^1H NMR spectrum.

Although treatment of **11e** with etheral $ZnCl_2$ affords a small amount of the desired acrylate (Scheme 3), unidentified decomposition products predominate in which loss of the methanethio signal was observed.

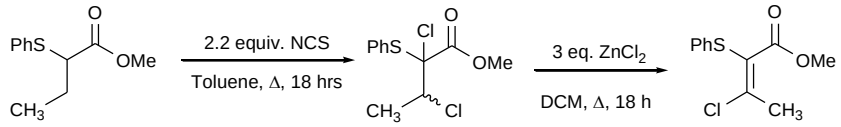


10e **11e** **6e**

Scheme 3

Preparation of Extended Chain β-Chloroacrylates

The ester **10f**[9] was treated under the conditions described previously for **10a & 10b** to give the dichloride **11f** as a 3:2 mixture of diastereomers (Scheme 4).

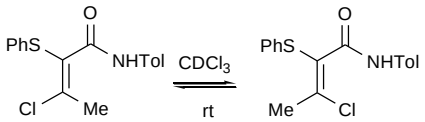


10f **11f** 3:2 **6f** 77%

Scheme 4

The mixed diastereomers of the crude dichloride **11f** were treated with 3 equivalents of $ZnCl_2$ in DCM under reflux for 18 h, and the crude β-chloroacrylate **6f** was isolated. Analysis of the crude material showed predominately one isomer of the β-chloroacrylate, tentatively assigned as *Z*, to have formed although a trace amount of the other isomer was also observed. After chromatography, **6f** was isolated as a single isomer in 77% yield (Scheme 4). This contrasts with what has been previously observed for the butenamides where mixtures of E and Z isomers were obtained directly from the NCS reaction, without exposure to $ZnCl_2$.[1] It is likely that the $ZnCl_2$ used in the decomposition of the dichloride **11f** catalyses the interconversion of the isomers of **6f** leading to the thermodynamically favoured isomer.

Interestingly, the E and Z isomers of **6g** are seen to interconvert in $CDCl_3$ when monitored by ^{1}H NMR spectroscopy over a prolonged period (Scheme 5). *E*-**6g** and *Z*-**6g** do not interconvert in the solid state.[10]



***Z*-6g** ***E*-6g**

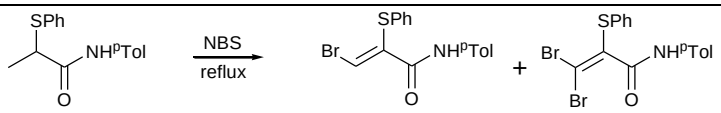
Scheme 5

Halogenation using NBS

To extend the scope of the halogenation process, it was decided to explore the reaction of *N*-tolyl-α-(phenylthio)propanamide **10c** with NBS. In general α-bromosulfides are more reactive but less stable than α-chlorosulfides, and thus have been used less frequently as synthetic intermediates.[11] However, most of the methods used for α-chlorosulfide preparation have been applied with varying degrees of success to the synthesis of α-bromosulfides. In the direct α-bromination of sulfides, bromine and NBS have been employed. Benzyl sulfide reacts with NBS to provide α-bromobenzyl benzylsulfide[11] which on distillation resulted in rapid decomposition to benzylbromide and other unidentified materials. An interesting example of γ-bromination was reported by Caputo *et al*;[12] the bromosulfonium ion is formed, however, as there is no α-hydrogen atom, γ-bromination occurs.

N-Tolyl-α-(phenylthio)propanamide **10c** was treated with NBS under three sets of reaction conditions, which had been investigated using NCS,[1] to allow comparison of the reactivity of the α-thioamide **10c** with NCS and NBS (Table 3). The optimum conditions for reaction with NBS were found to be treatment of **10c** under reflux with 2.2 equivalents of NBS in toluene or CCl_4 for 3-6 h. A 1:1 mixture of the β-bromoacrylamide **16c** and the β,β-dibromoacrylamide **17c** was isolated.

Table 3 Treatment of α-thioamide **10c** with NBS



10c **16c** **17c**

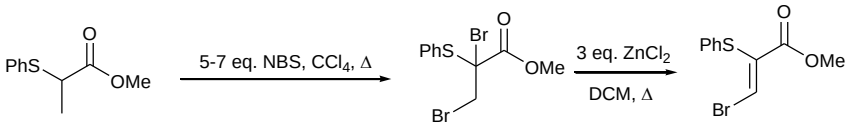
No. eq NBS	Temp (° C)	Solvent	Product Ratio	
			16c	**17c**
2.0	0-20	CCl_4	No reaction	
2.2	Reflux	CCl_4	1	1
2.2	Reflux	Toluene	1	1

These preliminary results indicated that extension of this work to bromo derivatives is possible.

Synthesis of the β-Bromoacrylate

Treatment of Methyl 2-(Phenylthio)propanoate 10a with NBS

Variation of the solvent, temperature, reaction time, concentration and number of equivalents of NBS was undertaken and it was found that use of 5-7 equivalents of NBS, added portionwise, in CCl_4 under reflux conditions gave predominantly the dibromide **18a** (Scheme 6). On some occasions, evidence for methyl 2-bromo-2-(phenylthio)propanoate **16a** was seen in the ^{1}H NMR spectrum of the crude product.



10a **18a** 99% **16a** 87%

Scheme 6

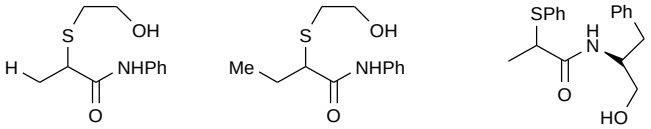
As with the dichloro compounds, the most significant feature of the ^{1}H NMR spectrum of the dibromide is the characteristic AB quartet for the methylene group. Unlike the dichlorides, however, the range of the AB quartet in the dibromide **18a** is quite large, from δ_H 3.58 to 4.21 (J_{AB} 11) indicating the alteration in the environment of the CH_2 protons on replacement of chlorine by the larger bromine substituent.

The decomposition of **18a** to the β-bromoacrylate **16a** was achieved employing the conditions developed for the decomposition of dichloride **11a** (Scheme 6). Compound **16a** is isolated as a pale yellow oil following chromatography and bulb to bulb distillation at reduced pressure. The characteristic shift of the β-proton in the ^{1}H NMR spectrum was seen at δ_H 7.93. Samples of **16a** were stored at room temperature for up to 3 months with no evidence of any decomposition by ^{1}H NMR spectroscopy.

As with the chloro derivative **6a**, only one isomer of the β-bromoacrylate **16a** was evident on both ^{1}H and ^{13}C NMR spectra. The isolated isomer was assigned *Z* by analogy to the β-chloroacrylates.

Investigation of the transformation of the α-thioamides bearing additional functional groups

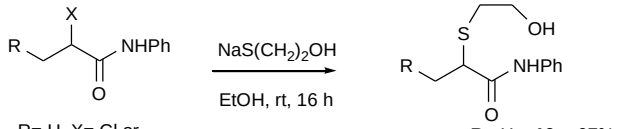
In order to broaden the scope of the stereoselective oxidative chlorination, we investigated the chlorination of functionalized sulfides such as **10g-i**, substrates which are interesting due to their potential to function as internal nucleophiles in intramolecular substitution reactions of β-chloroacrylamides.



10g **10h** **10i**

Use of sulfide substituent bearing a primary hydroxyl group

Two α-thioamides bearing a hydroxyl group on the sulfur substituent, *N*-phenyl-2-[2′-(hydroxyethyl)thio]propanamide **10g** and *N*-phenyl-2-[2′-(hydroxyethyl)thio]butanamide **10h**, were prepared by treatment of the corresponding α-haloamide[1] with the sodium salt of mercaptoethanol (Scheme 7).

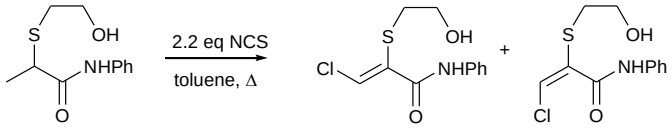


R= H, X= Cl or
R= Me, X= Br

R= H **10g** 67%
R= Me **10h** 92%

Scheme 7

Transformation of the α-thiopropanamide **10g** to the corresponding β-chloroacrylamide was possible, but the reaction was more sensitive than that of the simpler amides. Optimised conditions involved treatment of the propanamide **10g** with 2.2 equivalents of NCS in toluene under reflux conditions for 5 min on a 1-2 mmolar scale. Decomposition to various products occurred on prolonged heating. Purification by chromatography led to the isolation of the *Z* and *E* isomers of the β-chloroacrylamide **6g** in 33% and 13% yields respectively (Scheme 8).



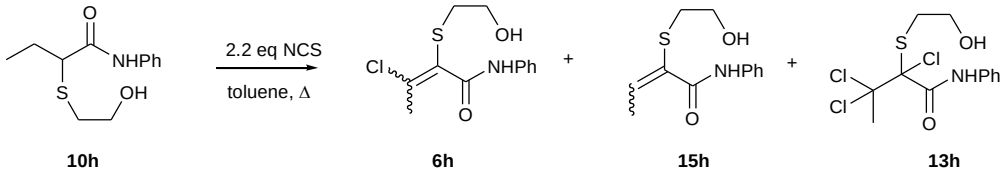
10g ***Z*-6g** 33% ***E*-6g** 13%

Scheme 8

Interestingly, for these substrates the previously observed *Z* stereoselectivity is not seen here. Possibly, the hydroxyl group influences the stereochemistry.

Formation of the *E* and *Z* β-chloroacrylamides from α-thiobutanamide **10h** using the conditions optimized for the chlorination of the propanamide derivative was also possible, albeit in decreased yields. On a 2 mmolar scale the reaction gave the isolated *Z* and *E* β-chloroacrylamides **6h** in yields of 34% and 22% respectively following chromatography. As is usual for extended chain amides, some Z-acrylamide **15h** was formed but was isolated together with an unknown compound in combined 8% yield. The trichloride **13h**, which is a product of further reaction of the β-chloroacrylamide with NCS, was also isolated in 18% yield (Scheme 9).

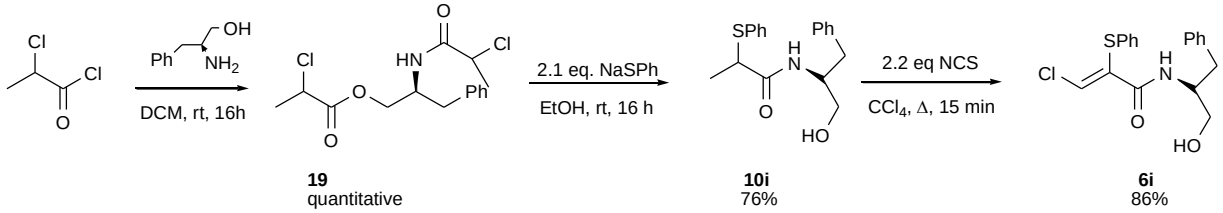
On a larger scale, the reaction with NCS is exothermic, so slow addition is required. Unfortunately, during slow addition, extensive decomposition occurs and the products are isolated in reduced yield- *Z*-β-chloroacrylamide ***Z*-6h** (17%), *E*-β-chloroacrylamide ***E*-6h** (8%) and *E* and *Z* acrylamides **15h** (12% combined).



Scheme 9

Use of amide substituent bearing a primary hydroxyl group

Treatment of (S)-phenylalaninol with 2 equivalents of 2-chloropropionyl chloride resulted in acylation of both the amino and hydroxyl groups, to give a complex mixture of diastereomers. However, the basic conditions used in the sulfenylation of the diacylated phenylalaninol **19** caused ester cleavage to give the desired propanamide **10i** as a mixture of diasteromers (Scheme 10).

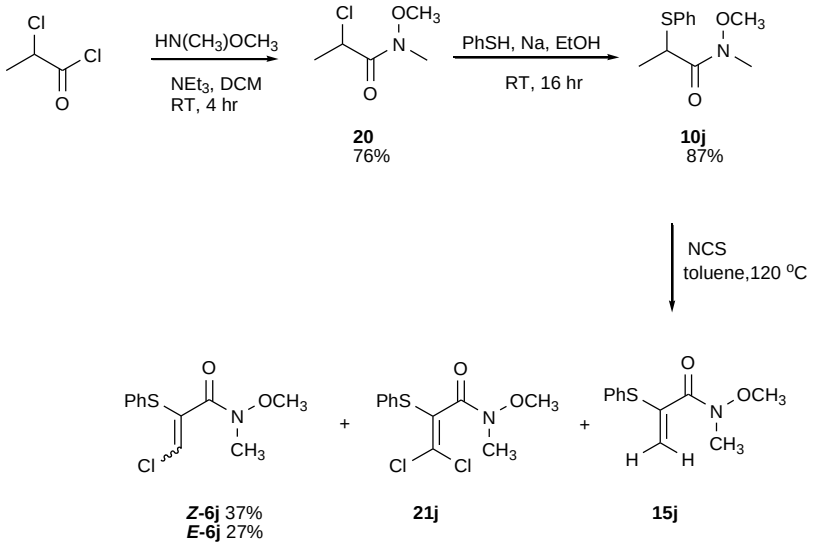


Scheme 10

Treatment of the α-thioamide **10i** with 2.2 equivalents of NCS in CCl_4 under reflux conditions for 15 minutes gave the *Z*-β-chloroacrylamide **6i** in 86% yield following chromatographic purification (Scheme 10).

Synthesis of the Weinreb Amide derivatives of the β-chloroacrylamides

Weinreb amides have been widely used in the literature as effective acylating reagents.[17-19] The Weinreb amide **20** was prepared as reported, [17] however triethylamine was used in place of pyridine to give the amide as a clear oil in 76% yield. The α-thioamide was then prepared as described previously[1] using thiophenol and sodium in ethanol for 18 hours. The α-thioamide **10j** was obtained as a colourless oil in 87% yield (Scheme 11).



Scheme 11

The α-thioamide **10j** was treated with 1.95 equivalents of NCS in toluene at 120 °C for 2.5 hours. Analysis of the crude reaction mixture by ^{1}H NMR spectroscopy showed complete conversion of the sulfide to a mixture of the *Z* and *E* β-chloroacrylamides **6j** in a ratio of 2:1. Some evidence for the acrylamide **15j** was also observed in this spectrum. The *E* and *Z* isomers are separable by chromatography and were isolated in yields of 27% and 37% respectively. The dichloroacrylamide **21j** was also isolated in 14% yield (Scheme 11).

Conclusion

The scope of stereoselective oxidative chlorination of thioamides to form the chloroacrylamides on treatment with NCS has been extended to include the analogous ester, nitrile and Weinreb amide series. Interestingly, chloride elimination is less facile in the ester and nitrile series than in the amide series, presumably due to the electronic impact of conformational factors. Thus, the direct product isolated in the ester and nitrile series is the dichloride, which is then transformed to the acrylate and acrylonitrile on treatment with $ZnCl_2$. Furthermore, the presence of hydroxyl groups on the sulfide and amide groups is tolerated. In addition, use of NBS in place of NCS leads to the corresponding bromide derivatives.

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. Acetone was distilled from potassium permanganate and toluene was distilled from sodium and stored over 4Å molecular sieves. Dimethylformamide was stored overnight over calcium hydride, then distilled and stored over 4 Å molecular sieves. Organic phases were dried using anhydrous magnesium sulphate. All commercial reagents, including *N*-chlorosuccinimide, were used without further purification.

^{1}H (300 MHz) and ^{13}C (75.5 MHz) NMR spectra were recorded on a Bruker (300 MHz) NMR spectrometer. ^{1}H (270 MHz) and ^{13}C (67.8 MHz) NMR spectra were recorded on a Jeol GSX (270 MHz) NMR spectrometer. ^{1}H (60 MHz) NMR spectra were recorded on a Jeol PMX-60SI spectrometer. All spectra were recorded at room temperature (~20^{o}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 analyzer. 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 (254nm) light detection, iodine staining, vanillin staining and ceric sulfate staining.

Nitrile Derivatives

Products of Treatment of 2-(Phenylthio)propionitrile 1 with NCS

3-Chloro-2-(phenylthio)propenonitrile 4,5, 2-(Phenylthio)propenonitrile 3 and 2,3-Dichloro-2-(Phenylthio)propionitrile 2

NCS (320 mg, 2.40 mmol) was added in one portion to a solution of the sulfide **1** (200 mg, 1.23 mmol) in toluene (4 ml). The flask was immediately immersed in an oil bath at 140 °C and heating was maintained for 18 h with stirring. The reaction mixture was cooled to 0 °C and the succinimide by-product removed by filtration. The solvent was evaporated at reduced pressure to give the crude product mixture of the *Z* and *E* 3-chloro-2-(phenylthio)propenonitriles **4** and **5**, 2-(phenylthio)propenonitrile **3**, 3-dichloro-2-(phenylthio)propionitrile **2** in a ratio of 1:1:1:8 by ^{1}H NMR spectroscopy (270 MHz). Evidence for both the *E* and *Z* β-chloroacrylonitriles was seen, the two compounds being present in equimolar amounts, each contributing approximately 10% of the reaction mixture. The crude reaction mixture was dissolved in DCM (4 ml) and a solution of $ZnCl_2$ (2.60 ml of 1.0 M solution in ether, 2.60 mmol) was added. The reaction solution was heated at reflux for 18 h. After cooling to room temperature, water (100 ml) was added and the phases separated. The organic layer was washed with water (100 ml) and brine (100 ml), dried and concentrated at reduced pressure to give the crude reaction product. This was then purified by chromatography on silica gel using ethyl acetate/hexane (5:95) as eluent to give a mixture of the *Z* and *E* β-chloroacrylonitriles **4** and **5** (126 mg, 52%) as a yellow oil in a ratio of 6:1 and approximately 10% of the dichloride **2**; ν_{max}/cm^{-1} (film) 2230 (CN), 1551, 1478, 1442, 1146; δ_H 7.00 (0.86H, s,

C*H*Cl= of one diastereomer), 7.14 (0.14H, s, C*H*Cl= of one diastereomer), 7.35-7.59 (5H, m, Ar*H*); δ_C 113.5 (*C*N of minor diastereomer), 115.9 (*C*N of major diastereomer), 128.5 (quaternary aromatic), 129.3 (aromatic *C*H), 129.8 (aromatic *C*H), 131.8 (*C*HCl= of minor diastereomer), 132.5 (*C*HCl= of major diastereomer), 134.3 (aromatic *C*H), 137.5 (S*C*= of minor diastereomer), 137.4 (S*C*= of major diastereomer).

Characteristic peaks for the acrylamide **3** and the dichloride **2** were observed and were as reported below.

Ester Derivatives

Methyl 2,3-dichloro-2-(phenylthio)propanoate 11a, Methyl 2-(Phenylthio)propenoate 15a and Methyl 2-chloro-2(phenylthio)propanoate 14a[4]

NCS (1.86 g, 13.93 mmol) was added in one portion to a stirred solution of the sulfide **10a** (1.30 g, 6.63 mmol) in toluene (26 ml). The flask was immediately lowered into a pre-heated oil bath at 130 °C. Heating was maintained for 4 h. The reaction solution was cooled to 0 °C and the succinimide by-product was removed by filtration. The toluene was evaporated at reduced pressure to give the crude dichloride **11a** as a yellow oil. The crude product was purified by chromatography on silica gel using ethyl acetate-hexane (gradient elution 10-20% ethyl acetate) to give the dichloride **11a** (1.53 g, 87%) as a clear oil; ν_{max}/cm^{-1} (film) 1753 (CO), 1440, 1286, 1258; δ_H 3.79 (3H, s, OCH_3), 3.90-4.05 (2H, ABq, *J* 12, CH_2Cl), 7.39-7.51 (3H, m, Ar*H*), 7.65-7.71 (2H, m, Ar*H*); δ_C 49.3 (*C*H_2Cl), 53.9 (O*C*H_3), 78.3 (S*C*Cl), 128.0 (quaternary aromatic), 129.2 (aromatic *C*H), 131.2 (aromatic *C*H), 137.3 (aromatic *C*H), 166.0 (*C*O); Exact mass calculated for $C_{10}H_{10}Cl_2O_2S$ $[M]^+$ 263.9779. Found 263.9793; 264 $[(M)^+$, 34%]. Evidence for the acrylate **15a** was seen in some crude NMR spectra at δ_H 3.82 (s, OCH_3), 5.24 (s, one of CH_2) and 6.33 (s, one of CH_2).

The NMR spectra of some crude reaction mixtures also showed evidence of the α-chloro sulfide **14a** at δ_H 2.01 (s, CH_3-3) and 3.72 (s, OCH_3).

Methyl 2-chloro-2-(phenylthio)propanoate 14a[4]

1. Use of one equivalent of NCS

NCS (75 mg, 0.56 mmol) was added in one portion to a stirred solution of the sulfide **10a** (100 mg, 0.51 mmol) in toluene (2 ml) at room temperature. The resulting solution was stirred at room temperature for 18 h before cooling to 0 °C. The succinimide by-product was removed by filtration to give the α-chloro sulfide **14a** and approximately 30% unreacted sulfide **10a**. No further purification was conducted and characteristic signals for **14a** could be distinguished; δ_H 2.01 (3H, s, C*H*$_3$-3), 3.72 (3H, s, OC*H*$_3$), 7.21-7.62 (5H, m, Ar*H*); m/z (ESI) 230 [$(M)^+$, 6%], 194 [$(M^+$-HCl), 17%].

2. Use of two equivalents of NCS:

NCS (150 mg, 1.12 mmol) was added in one portion to a stirred solution of the sulfide **10a** (100 mg, 0.51 mmol) in toluene (2 ml) at room temperature. The resulting solution was stirred at room temperature for 18 h before cooling to 0^{o}C. The succinimide by-product was removed by filtration to give the α-chloro sulfide **14a**. No further purification was conducted and spectral characteristics were as previously reported. A trace of the acrylate was seen at δ_H 5.24 and 6.33 as reported previously.

Ethyl 2,3-dichloro-2-(phenylthio)propanoate 11b

NCS (3.42 g, 25.39 mmol) was added in one portion to a solution of the sulfide **10b** (2.42 g, 11.54 mmol) in toluene (50 ml). The flask was immediately immersed in an oil bath at 124 °C and heating was maintained for 20 h with stirring. The reaction mixture was cooled to 0 °C and the succinimide by-product removed by filtration. The crude product was purified by chromatography on silica gel using ethyl acetate-hexane (30:70) as eluent to give the dichloride **11b** (2.74 g, 85%) as a yellow oil; Found C, 47.70; H, 4.59; Cl, 25.24; S, 11.35. $C_{11}H_{12}Cl_2O_2S$ requires C, 47.32; H, 4.33; Cl, 25.40; S, 11.48. ν_{max}/cm^{-1} (film) 1747 (CO), 1441, 1256, 1185; δ_H 1.29 (3H, t, *J* 7, C*H*$_3$), 3.82-4.01 (2H, ABq, *J* 12, CCl*H*$_2$), 4.26 (2H, q, *J* 7, OC*H*$_2$), 7.33-7.52 (3H, m, Ar*H*), 7.63-7.72 (2H, m, Ar*H*); δ_C 13.8 (CH_2CH_3), 49.1 (*C*ClH_2), 63.5 (O*C*H$_2$), 78.3 (S*C*Cl), 127.5 (quaternary aromatic), 128.9 (aromatic *C*H), 131.0 (aromatic *C*H), 137.3 (aromatic *C*H), 165.4 (*C*O); Exact mass calculated for $C_{11}H_{12}Cl_2O_2S$ $[M]^+$ 277.9935. Found 277.9940; 282, 280, 278 (M^+, 67%), 243 (24, M^+-Cl), 205, 207 (85, M^+-COOEt), 170 (28, M^+-COOEt-Cl), 135 (87, M^+-COOEt-Cl_2), 109 (100, $[SPh]^+$).

Methyl *Z*-3-Chloro-2-(phenylthio)propenoate 6a from the Sulfide 10a

NCS (23.00 g, 22.44 mmol) was added to a solution of the sulfide **10a** (2.00 g, 10.20 mmol) in toluene (40 ml). The reaction flask was immediately lowered into a pre-heated oil bath at 128 °C and the reaction solution refluxed for 16 h. After cooling to 0 °C, the succinimide by-product was removed by filtration and the toluene evaporated at reduced pressure. ^{1}H NMR spectroscopy (60 MHz) of this material showed complete conversion of the sulfide **10a** to the corresponding dichloride **11a**. The crude dichloride **11a** was dissolved in DCM (40 ml) and a solution of $ZnCl_2$ in ether (31.00 ml of 1M soln., 31.00 mmol) added. The resulting solution was then heated at reflux for 16 h when, after cooling to room temperature, water (100 ml) was added and the phases separated. The organic layer was washed with water (100 ml) and brine (100 ml), dried and concentrated at reduced pressure to give the crude product mixture which appeared to be of good quality by NMR. The crude product was purified by chromatography on silica gel using ethyl acetate-hexane (10:90) as eluent to give the β-chloroacrylate **6a** (1.53 g, 66% from sulphide) as a yellow oil. A portion of this material was purified by bulb to bulb distillation (100 °C at 0.02 mm Hg); Found C, 52.83; H, 4.09; Cl, 15.62; S, 13.90. $C_{10}H_9ClO_2S$ requires C, 52.52; H, 3.97; Cl, 15.50; S, 14.02. ν_{max}/cm^{-1} (film) 1732 (CO), 1557, 1271, 1242, 741; δ_H 3.67 (3H, s, OC*H*$_3$), 7.18-7.38 (5H, m, Ar*H*), 7.71 (1H, s, C*H*Cl=); δ_C 52.8 (O*C*H$_3$), 127.7 (aromatic *C*H), 129.3 (aromatic *C*H), 129.9 (aromatic *C*H), 133.3 (quaternary aromatic or S*C*=, one signal observed for 2 quaternary carbons), 138.0 (*C*HCl=), 163.7 (*C*O); MS *m/z* 228, 230 (M^+, 100%), 192 (18, M^+-HCl), 161 (35), 149 (42), 134 (100, $[PhS\text{-}C{=}CH]^+$), 110 (48), 109 (42, $[SPh]^+$); isotopic Cl pattern observed; 228, 230 (3:1 ^{35}Cl:^{37}Cl).

A mixed fraction (least polar, 90 mg) consisting of the β-chloroacrylate **6a** and the trichloride **13a** was also isolated in a ratio of **6a**:**13a** of 1:2. Characteristic signals for the trichloride were seen at δ_H 3.72 (3H, s, OC*H*$_3$) and 6.76 (1H, s, C*H*Cl$_2$-).

A further fraction (most polar, 25 mg) was also isolated and was shown to be the bis sulfide **12a** with characteristic signals seen at δ_H 3.73 (3H, s, OC*H*$_3$), 7.18-7.58 (10H, m, Ar*H*), 8.43 (1H, s, C*H*SPh=); Exact mass calculated for $C_{16}H_{14}O_2S_2$ $[M]^+$ 302.0435.

Found 302.0430; 302 (M^+, 100%), 193 (16, M^+-SPh), 161 (16), 134 (38, $[PhS\text{-}C{=}CH]^+$), 109 (17, $[SPh]^+$), 51 (12).

Methyl *Z*-3-chloro-2-(phenylthio)propenoate 6a from the Dichloride 11a

A solution of $ZnCl_2$ in ether (71.00 ml of 1M soln., 71.00 mmol) was added to a stirred solution of the dichloride **11a** (6.27 g, 23.70 mmol) in DCM (120 ml). The reaction solution was then heated at reflux for 18 h, then water (100 ml) was added and the phases separated. The organic layer was washed with water (100 ml) and brine (100 ml), dried and concentrated at reduced pressure to give the crude product which was purified by chromatography on silica gel using ethyl acetate-hexane (gradient elution 0-5% ethyl acetate) as eluent to give the β-chloroacrylate **6a** (3.65 g, 70%) as a yellow oil. Spectral details were as previously reported. A mixed fraction (0.34 g) consisting of a mixture of the β-chloroacrylate **6a** and the bis sulfide **12a** was also isolated with a ratio of **6a**:**12a** of 2:3. Again, spectral details were as previously reported.

Ethyl *Z*-3-chloro-2-(phenylthio)propenoate 6b

A solution of $ZnCl_2$ in ether (18.00 ml of 1M soln., 18.00 mmol) was added to a stirred solution of the dichloride **11b** (2.00 g, 7.20 mmol) in DCM (40 ml) at room temperature. The reaction solution was stirred for 18 h, then water (50 ml) was added and the phases separated. The organic layer was washed with water (50 ml) and brine (50 ml), dried and concentrated at reduced pressure to give the crude β–chloroacrylate **6b**. The crude product was purified by chromatography on silica gel using ethyl acetate-hexane as eluent to give the β–chloroacrylate **6b** (1.25 g, 71%) as a clear oil; Found C, 54.56; H, 4.50; Cl, 14.90; S, 13.02. $C_{11}H_{11}ClO_2S$ requires C, 54.43; H, 4.57; Cl, 14.61; S, 13.21. ν_{max}/cm^{-1} (film) 1728 (CO), 1560, 1267, 1242; δ_H 1.09 (3H, t, *J* 7, C*H*$_3$), 4.10 (2H, q, *J* 7, OC*H*$_2$), 7.20-7.51 (5H, m, Ar*H*), 7.64 (1H, s, C*H*Cl=); δ_C 13.7 (CH_2CH_3), 62.0 (OCH_2), 127.2 (aromatic *C*H), 128.7 (aromatic *C*H), 129.2 (aromatic *C*H), 130.1 (quaternary aromatic or S*C*=), 131.7 (quaternary aromatic or S*C*=), 136.9 (*C*HCl=), 163.2 (*C*O); MS *m/z* 242, 244 (M^+, 86%), 207 (34, M^+-Cl), 206 (41, M^+-HCl), 178 (44), 161 (62, M^+-HCl-OEt), 135 (100), 134 (99, $[PhS\text{-}C{=}CH]^+$), 109 (81, $[SPh]^+$), 77 (70); isotopic Cl pattern observed; 242, 244 (3:1 ^{35}Cl:^{37}Cl).

Methyl 2,3-dichloro-2-(*n*-butylthio)propanoate 11d, Methyl *Z*-3-chloro-2-(*n*-butylthio)propenoate 6d and Methyl 2,3-di-(*n*-butylthio)propanoate 12d

NCS (636 mg, 4.77 mmol) was added to a solution of the sulfide **10d** (400 mg, 2.27 mmol) in toluene (8 ml). The reaction solution was immediately lowered into a pre-heated oil bath at 130 °C. After 18 h heating under reflux, the reaction solution was cooled to 0 °C and the succinimide was removed by filtration. The toluene was removed by evaporation at reduced pressure to give the crude product, a 2: 1 mixture of the β-chloroacrylate **6d**: dichloride **11d**. Characteristic signals for the dichloride **11d** were seen at 4.01-4.20 (ABq, *J* 10). The crude reaction product was dissolved in DCM (3 ml) and $ZnCl_2$ (1.80 ml of 1M soln. in ether) added. The resulting solution was heated at reflux for 16 h then water (5 ml) was added and the phases separated. The organic layer was washed with water (5 ml) and brine (5 ml), dried and concentrated at reduced pressure to give the crude β-chloroacrylate **6d** which was purified by chromatography on silica gel using ethyl acetate-hexane (5:95) as eluent to give the β-chloroacrylate **6d** (238 mg, 51%) as a colourless oil; Found C, 46.48; H, 6.49; Cl, 16.70; S, 15.33. $C_8H_{13}ClO_2S$ requires C, 46.04; H, 6.28; Cl, 16.99; S, 15.36; ν_{max}/cm^{-1} (film) 1729 (CO), 1556, 1239; δ_H 0.90 (3H, t, *J* 7, C*H*$_3$-4'), 1.35-1.63 (4H, m, C*H*$_2$-3', C*H*$_2$-2'), 2.86 (2H, t, *J* 7, SC*H*$_2$), 3.83 (3H, s, OC*H*$_3$), 7.53 (1H, s, C*H*Cl=); δ_C 13.8 (*C*H$_3$-4'), 21.9 (*C*H$_2$-3'), 32.2 (*C*H$_2$-2'), 33.2 (S*C*H$_2$), 53.1 (O*C*H$_3$), 136.2 (*C*HCl=). Quaternary carbons (S*C*= and *C*O) not observed; Exact mass calculated for $C_8H_{13}ClO_2S$ $[M]^+$ 208.0325. Found 208.0310; 208, 210 (M^+, 7%), 173 (11, M^+-Cl), 157 (100), 143 (74), 135 (54), 57 (58); isotopic Cl pattern observed; 208, 210 (3:1 ^{35}Cl:^{37}Cl).

A signal corresponding to the bis sulfide compound **12d** (trace amount) was also seen at δ_H 8.08. The molecular ion of this compound was also seen in the mass spectrum at 262 (6%).

Attempted preparation of methyl *Z*-3-chloro-2-(methylthio)acrylate 6e

Treatment of methyl 2-(methylthio)propionate **10e** (2.0 g, 14.9 mmol) with NCS (3.88 g, 29.1 mmol) in toluene (40 mL) at 90 °C for 2 h afforded a material assumed to be the *vic*-dichloride, methyl 2,3-dichloro-2-(methylthio)propionate **11e**, on the basis of the ^1H

NMR spectrum. Yield 2.65 g (87%). δ_H (300 MHz, $CDCl_3$) 5.07-4.95 (m, 2 H, C*H*$_2$), 3.87 (s, 3 H, OC*H*$_3$), 2.12 (s, 3 H, SC*H*$_3$).

Treatment of this material with $ZnCl_2$ under a range of conditions (10 eq. $ZnCl_2$, 36 °C, 18 h; 10 eq., RT, 18 h; 10 eq., RT, 4 h; 2 eq., RT, 18 h) afforded only traces of the desired chloroacrylate **6e** accompanied by a complex mixture of decomposition products with no SCH_3 signal in the ^{1}H NMR. On a 1.5 g scale, under the first conditions described above, a 4% isolated yield of the desired material was obtained in an impure state which was characterised only by ^{1}H NMR. δ_H (300 MHz, $CDCl_3$) 3.83 (s, 3 H, OC*H*$_3$), 2.39 (s, 3 H, SC*H*$_3$).

Methyl 2,3-dichloro-2-(phenylthio)butanoate 11f

NCS (668 mg, 5.00 mmol) was added in one portion to a solution of methyl 2-(phenylthio)butanoate **10f** (500 mg, 2.38 mmol) in toluene (10 ml). The reaction solution was immediately lowered into a pre-heated oil bath at 130 °C. After 18 h heating under reflux, the reaction solution was cooled to 0 °C and the succinimide was removed by filtration. The toluene was removed by evaporation at reduced pressure to give the crude dichloride **11f** (546 mg, 83%) as a 3:2 mixture of diastereomers which was used without further purification; δ_H 1.60 (1.8H, d, *J* 6, C*H*$_3$ of major diastereomer), 1.84 (1.2H, d, *J* 6, C*H*$_3$ of minor diastereomer), 3.58 (1.8H, s, OC*H*$_3$ of major diastereomer), 3.60 (1.2H, s, OC*H*$_3$ of minor diastereomer), 4.78-4.90 (1H, 2 overlapping q, C*H*Cl-).

Methyl 3-Chloro-2-(phenylthio)butenoate 6f

A solution of $ZnCl_2$ (4.6 ml of 1.0M soln. in ether, 4.60 mmol) was added to a solution of the dichloride **11f** (107 mg, 0.39 mmol) in DCM (2 ml). The reaction solution was heated at reflux for 18 h before work-up as outlined for **6a** to give the crude β-chloroacrylate which was purified by chromatography on silica gel using ethyl acetate-hexane (5:95) as eluent to give methyl 3-chloro-2-(phenylthio)butenoate **6f**, tentatively assigned as *Z*, (73 mg, 77%) as a yellow oil; Found C, 54.18; H, 4.66; Cl, 14.27; S, 13.46. $C_{11}H_{11}ClO_2S$ requires C, 54.43; H, 4.57; Cl, 14.61; S, 13.21; δ_H 2.43 (3H, s, =CC*H*$_3$), 3.49 (3H, s, OC*H*$_3$), 7.20-7.39 (5H, m, Ar*H*); δ_C 25.4 (*C*H$_3$), 52.4 (O*C*H$_3$), 127.5 (aromatic *C*H), 129.2 (aromatic *C*H), 130.8 (aromatic *C*H), 133.3 (quaternary aromatic or

S*C*= or *C*Cl=), 136.7 (quaternary aromatic or S*C*= or *C*Cl=), 143.5 (quaternary aromatic or S*C*= or *C*Cl=), 165.2 (*C*O); MS *m/z* 242, 244 (M^+, 20), 226 (30), 155 (43), 91 (46), 77 (100); isotopic Cl pattern observed; 242, 244 (3:1 ^{35}Cl:^{37}Cl).

A second compound was also seen in the NMR, possibly the *E* isomer of the β-chloroacrylate, at δ_H 2.45 (3H, s, =CCH_3), 3.65 (3H, s, OCH_3) and at δ_C 24.5, 126.2, 129.6 and 167.7.

Halogenation using NBS

Treatment of *N*-4′-methylphenyl-2-(phenylthio)propanamide 10c with NBS

NBS (0.41 g, 2.3 mmol) was added to a solution of *N*-4′-methylphenyl-2-(phenylthio)propanamide **10c** (0.30 g, 1.1 mmol) in toluene (7 ml) and the reaction flask was immersed in an oil bath at 130 °C. After stirring for 6 h the reaction mixture was cooled to 0 °C and the succinimide by-product was removed by filtration. The filtrate was evaporated to give a complex mixture of products (0.39 g). Purification by chromatography using ethyl acetate-hexane (15:85) as eluent followed by preparative TLC using ethyl acetate-hexane (15:85) as eluent gave two major fractions which contained compounds which were tentatively assigned as; *N*-4′-methylphenyl-3-bromo-2-(phenylthio)propenamide **16c** (10 mg) as a colourless oil; ν_{max}/cm^{-1} (neat) 3318 (br NH), 1676 (CO α,β-unsaturated amide); δ_H 2.31 (3 H, s, ArCH_3), 7.07-7.47 (9 H, m, Ar*H*), 8.31 (1 H, s, C*H*Br=); MS *m/z* 347 (M^+, 40 %), 239 (57, M^+-PhS-H), 212 (20, $[PhS=C=CBr]^+$), 134 (67, $[PhS=C=CH]^+$), isotopic bromine pattern observed 347, 349 (1:1 ratio ^{79}Br:^{81}Br); *N*-4′-methylphenyl-3,3-dibromo-2-(phenylthio)propenamide **17c** (10 mg) was also recovered as a colourless oil; ν_{max}/cm^{-1} (neat) 3298 (br NH), 1659, 1604 (CO amide); δ_H 2.27 (3 H, s, ArCH_3), 7.03-7.65 (9 H, m, Ar*H*); MS *m/z* 425 (M^+, 22 %), 212 (100, $[PhS=C=CBr]^+$), 91 (48, $[Tol]^+$); isotopic bromine pattern observed 425, 427, 429 (1:2:1 ratio ^{79}Br:^{81}Br), 212, 214 (1:1 ratio ^{79}Br:^{81}Br).

Methyl 2,3-dibromo-2-(phenylthio)propanoate 18a and Methyl 2-bromo-2-(phenylthio)propanoate 16a

NBS (454 mg, 2.55 mmol) was added to a solution of the sulfide **10a** (200 mg, 1.02 mmol) in CCl_4 (4 ml). The reaction flask was immediately lowered into a pre-heated oil bath at 90 °C. After heating under reflux for 3 h, the flask was removed from the oil bath and a sample (1 ml) removed. A ^{1}H NMR spectrum (60 MHz) was recorded (in CCl_4) which showed the reaction to be approximately 78% complete. The NMR sample was returned to the reaction flask and a further addition of NBS (454 mg, 2.55 mmol) was made. The reaction vessel was again lowered into the pre-heated oil bath and reflux was maintained for a further 18 h. ^{1}H NMR spectroscopy (60 MHz in CCl_4) showed 95% conversion to the dibromide **18a**. A final addition of NBS (200 mg, 1.10 mmol) was made and after refluxing for a further 6 h, the reaction was complete by ^{1}H NMR spectroscopy (60 MHz). The reaction solution was filtered to remove the succinimide by-product and the CCl_4 was evaporated at reduced pressure to give the crude dibromide **18a** as a yellow oil. The crude product was purified by chromatography on silica gel to give the dibromide **18a** (274 mg, 76%) as clear oil; Found C, 34.00; H, 2.81; Br, 45.26; S, 9.22. $C_{10}H_{10}Br_2O_2S$ requires C, 33.92; H, 2.85; Br, 45.14; S, 9.06. ν_{max}/cm^{-1} (film) 1747 (CO), 1439, 1269, 1165, 753; δ_H 3.58-3.63 (1H, H_A of ABq, *J* 11, one of C*H*$_2$Br), 3.90 (3H, s, OC*H*$_3$), 4.16-4.21 (1H, H_B of ABq, *J* 11, one of C*H*$_2$Br), 7.39-7.58 (3H, m, Ar*H*), 7.74-7.82 (2H, m, Ar*H*); δ_C 36.7 (*C*H$_2$Br), 54.1 (O*C*H$_3$), 69.3 (S*C*Br), 128.2 (quaternary aromatic), 129.0 (aromatic *C*H), 130.9 (aromatic *C*H), 137.0 (aromatic *C*H), 166.2 (*C*O); Exact mass calculated for $C_{10}H_{10}Br_2O_2S$ $[M]^+$ 353.8748. Found 353.8747; 354 (M^+, 1%), 273, 275 (19, M^+-Br), 194 (45, M^+-Br_2), 163 (5, M^+-Br_2-OCH_3), 135 (100, $[PhS\text{-}C{=}CH_2]^+$), 109 (20, $[SPh]^+$), 91 (55).

When this reaction was repeated using 3.00 g (15.31 mmol) of **10a**, the dibromide **18a** was isolated in 99% yield. No further purification of this material was required.

A characteristic signal for methyl 2-bromo-2-(phenylthio)propanoate **16a** was seen in some crude NMR spectra at δ_H 2.83 (s).

Methyl *Z*-3-bromo-2-(phenylthio)propenoate 16a from the dibromide 18a

A solution of $ZnCl_2$ in ether (45.60 ml of 1M soln., 45.60 mmol) was added to a stirred solution of the dibromide **18a** (5.38 g, 15.20 mmol) in DCM (110 ml). The reaction solution was then heated under reflux for 18 h, then water (100 ml) was added and the

phases separated. The organic layer was washed with water (100 ml) and brine (100 ml), dried and concentrated at reduced pressure to give the crude product which was purified by chromatography on silica gel using ethyl acetate-hexane (gradient elution 0-5% ethyl acetate) as eluent to give the β-bromoacrylate **16a** (3.61 g, 87%) as a yellow oil. A portion of this material was purified by bulb to bulb distillation (110 °C at 0.02 mm Hg); Found C, 43.95; H, 3.36; Br, 31.25; S, 11.70. $C_{10}H_9BrO_2S$ requires C, 43.97; H, 3.32; Br, 29.25; S, 11.74. ν_{max}/cm^{-1} (film) 1732 (CO), 1554, 1434, 1258, 741; δ_H 3.62 (3H, s, OC*H*$_3$), 7.19-7.38 (5H, m, Ar*H*), 7.93 (1H, s, C*H*Cl=); δ_C 52.7 (O*C*H$_3$), 127.3 (aromatic *C*H or S*C*=), 128.2 (aromatic *C*H or S*C*=), 129.4 (aromatic *C*H), 130.1 (aromatic *C*H), 133.2 (quaternary aromatic or S*C*=), 134.7 (quaternary aromatic or S*C*=), 163.5 (*C*O); Exact mass calculated for $C_{10}H_9BrO_2S$ $[M]^+$ 271.9507. Found 271.9508; 274 (M^+ Br^{81}, 24%), 272 (M^+ Br^{79}, 26), 149 (23), 134 (100, M^+-Br-COOMe), 109 (32, $[SPh]^+$), 59 (26).

Use of sulfide bearing a primary hydroxyl group

***N*-Phenyl-2-[2′-(hydroxyethyl)thio]propanamide 10g**

Mercaptoethanol (2.3 ml, 32.8 mmol) was added to a freshly prepared solution of sodium ethoxide [made from sodium (1.38 g, 49.3 mmol) in dry ethanol (100 ml) at 0 °C] while stirring under nitrogen. The resulting solution was stirred for 20 minutes when *N*-phenyl-2-chloropropanamide **22g** (4.10 g, 22.4 mmol) was added gradually over 15 minutes. Following stirring for 16 h, the reaction was quenched by addition of water (50 ml) and DCM (30 ml). The phases were separated and the aqueous layer was extracted with DCM (2 x 30 ml). The combined organic layers were washed with NaOH (1M, 2 x 50 ml), water (100 ml) and brine (100 ml), dried and concentrated to give a yellow solid (4.93 g, 98% crude). Recrystallisation from ether-hexane (20:80) gave the sulfide **10g** (3.47 g, 67%) as a white, crystalline solid; mp 70-72 °C; Found C, 58.81; H, 6.77; N, 6.22; S, 14.43. $C_{11}H_{15}NO_2S$ requires C, 58.64; H, 6.71; N, 6.22; S, 14.23; ν_{max}/cm^{-1} (KBr) 3248, 1664, 1601; δ_H 1.52 (3 H, d, *J* 7, C*H*$_3$-3), 2.69-2.96 (3 H, m, C*H*$_2$S, O*H*), 3.63 (1 H, q, *J* 7, C*H*-2), 3.79-3.88 (2 H, m, C*H*$_2$O), 7.09-7.56 (5 H, m, Ar*H*), 8.80 (1 H, br s, N*H*); δ_C 18.4 (*C*H$_3$-3), 34.4 (*C*H$_2$S), 44.9 (*C*H-2), 61.8 (*C*H$_2$O), 120.0, 124.6, 129.1 (aromatic *C*H), 137.7 (quaternary aromatic *C*), 171.1 (*C*O); MS *m/z* 225 (M^+, 2%), 207 (5), 149 (20), 135 (3).

***N*-Phenyl-2-[2′-(hydroxyethyl)thio]butanamide 10h**

This was prepared following the procedure described for sulfide **10g** using *N*-phenyl-2-bromobutanamide **22h** (7.90 g, 32.6 mmol), mercaptoethanol (2.5 ml, 35.9 mmol), sodium (1.58 g, 68.5 mmol) and dry ethanol (100 ml) to give the sulfide (7.81 g, 100% crude). Trituration from cold hexane gave the sulfide **10h** (7.22 g, 92%) as an off-white, crystalline solid; mp 71-73 °C; Found C, 59.83; H, 7.23; N, 6.06; S, 13.14. $C_{12}H_{17}NO_2S$ requires C, 60.22; H, 7.16; N, 5.85; S, 13.40; ν_{max}/cm^{-1} (KBr) 3388 , 1670, 1604; δ_H 1.06 (3H, t, *J* 7, CH_3-4), 1.70-1.84 (1H ,m, C$H_A$$H_B$-3), 1.92-2.08 (1H, m, C$H_A$$H_B$-3), 2.68-2.88 (2H, m, C$H_2$S), 2.92-2.97 (1H, br t, O*H*), 3.45 (1H, t, *J* 7, SC*H*-2), 3.78-3.81 (2H, m, CH_2O), 7.08-7.58 (5H, m, Ar*H*), 8.81 (1H, br s, N*H*); δ_C 12.0 (*C*H_3-4), 26.0 (*C*H_2-3), 34.5 (*C*H_2S), 52.3 (*C*H-2), 61.8 (*C*H_2O), 120.0, 124.6, 129.0 (aromatic *C*H), 137.7 (quaternary aromatic *C*), 170.2 (*C*O); MS *m/z* 239 (M^+, 1 %), 179 (45), 166 (55), 151 (70), 124 (100).

***N*-Phenyl-*Z*-3-chloro-2-[2′-(hydroxyethyl)thio]propenamide *Z*-6g and *N*-phenyl-*E*-3-chloro-2-[2′-(hydroxyethyl)thio]propenamide *E*-6g**

NCS (3.65 g, 27.3 mmol) was added in one portion to a solution of **10g** (3.00 g, 13.3 mmol) in toluene (60 ml) at 130 °C. Reaction was complete after 5 min (by TLC analysis) to give a crude mixture of acrylamides (4.23 g) (*ca*. 60% of mixture) and several unidentified components. Purification by chromatography using ethyl acetate-hexane (7:93) to (30:70) as eluent gave β-chloroacrylamide **6g** (tentatively assigned as *E*) (0.45 g, 13%) (Rf 0.5 using ethyl acetate-hexane (25:75) as eluent) as a yellow oil (which seems to bind a molecule of water see MS); Found C, 50.93; H, 4.34; N, 5.46. $C_{11}H_{12}ClNO_2S$ requires C, 51.26; H, 4.69; N, 5.43; ν_{max}/cm^{-1} (neat) 3336, 1668, 1598; δ_H H_2O peak seen at 1.70-1.90 (br s), 2.56 (1H, s, O*H*), 3.15 (2H, t, *J* 7, CH_2S), 3.67 (2H, t, *J* 7, CH_2O), 7.14-7.66 (5H, m, Ar*H*), 7.97 (1H, s, C*H*Cl=), 9.08 (1H, br s, N*H*); δ_C 36.7 (*C*H_2S), 42.7 (*C*H_2O), 120.2, 125.1, 129.2 (aromatic *C*H and S*C*=), 130.9, 137.2 (quaternary aromatic *C*), 140.7 (*C*HCl=), 160.6 (*C*O); MS *m/z* 275 ($M^+ + H_2O$, 8 %), 240 (10, $M^+ + H_2O$ -Cl), 163 (100, $M^+ + H_2O$ -$[S(CH_2)_2OH]^+$); isotopic Cl pattern observed; 275, 277 (3:1 ratio ^{35}Cl:^{37}Cl) and β-chloroacrylamide **6g** (tentatively assigned as *Z*) (1.14

g, 33 %) (Rf 0.1) as a colourless oil; δ_H 2.56 (1H, br s, O*H*), 2.99 (2H, t, *J* 6, C*H*$_2$S), 3.79 (2H, t, *J* 6, C*H*$_2$O), 7.12-7.64 (5H, m, Ar*H*), 7.85 (1H, s, C*H*Cl=), 9.33 (1H,br s, N*H*); δ_C 37.2 (*C*H$_2$S), 60.4 (*C*H$_2$O), 120.2, 125.0, 129.0 (aromatic *C*H), 131.7, 137.3 (quaternary aromatic *C* and S*C*=), 139.6 (*C*HCl=), 161.4 (*C*O); Exact mass calculated for $C_{11}H_{12}ClNO_2S$ $[M]^+$ 257.02773. Found 257.02451; 257 (M^+ ,18 %), 239 (18, M^+ -Cl), 204 (58), 178 (43), 93 (100, $[NH_2Ph]^+$), isotopic Cl pattern observed; 257, 259 (3:1 ratio ^{35}Cl:^{37}Cl).

Treatment of *N*-phenyl-2-[2′-(hydroxyethyl)thio]butanamide 10h with NCS

This was prepared following the procedure described for **6g** using *N*-phenyl-2-[2′-(hydroxyethyl)thio]butanamide **10h** (0.50 g, 2.09 mmol), NCS (0.65 g, 4.83 mmol) and toluene (15 ml) at 130 °C. After stirring for 5 min the reaction was complete (by TLC analysis) giving a crude mixture of products. Purification by chromatography using ethyl acetate-hexane (30:70) as eluent gave *N*-phenyl-*E*-3-chloro-2-[2′-(hydroxyethyl)thio]butanamide **6h** (tentatively assigned as *E*)(Rf 0.6 using ethyl acetate-hexane (25:75) as eluent) (128 mg, 22 %) as a colourless oil; ν_{max}/cm^{-1} (neat) 3278, 1651, 1598; δ_H 2.48 (3H, s, C*H*$_3$-4), 2.94 (2H, dd, *J* 5, 5, C*H*$_2$S), 3.80 (2H, dd, *J* 5, 5, C*H*$_2$O), 7.15 (1H, t, *J* 8, *H*-4′), 7.35 (2H, dd, *J* 8, 8, *H*-3′ and *H*-5′), 7.57 (2H, d, *J* 8, *H*-2′ and *H*-6′), 8.74 (1H, br s, N*H*); δ_C 25.5 (*C*H$_3$-4), 36.6 (*C*H$_2$S), 61.1 (*C*H$_2$O), 119.9, 124.9 (aromatic *C*H), 126.7 (probably S*C*=), 129.1 (aromatic *C*H), 137.5 (quaternary aromatic *C*), 144.5 (*C*Cl=), 163.6 (*C*O); Exact mass calculated for $C_{12}H_{14}ClNO_2S$ $[M]^+$ 271.04338. Found 271.04357; 271 (M^+, 1 %), 235 (2, M^+-HCl), 151 (85, M^+-CONHPh), 124 (100); isotopic Cl pattern observed; 271, 273 (3:1 ratio ^{35}Cl:^{37}Cl); and *N*-phenyl-*Z*-3-chloro-2-(2′-hydroxy)ethylthiobutanamide **6h** (tentatively assigned as *Z*) (191 mg, 34%) (Rf 0.5) as a brown solid; mp 91-93 °C; δ_H 2.42 (3H, s, C*H*$_3$-4), 2.91 (2H , dd, *J* 5, 5, C*H*$_2$S), 3.10-3.50 (1H, br s, O*H*), 3.84 (2H, dd, *J* 5, 5, C*H*$_2$O), 7.11 (1H, t, *J* 8, *H*-4′), 7.30 (2H, t, *J* 8, *H*-3′ and *H*-5′), 7.57 (2H, d, *J* 8, *H*-2′ and *H*-6′), 8.33 (1H, br s, N*H*); δ_C 24.2 (*C*H$_3$-4), 37.0 (*C*H$_2$S), 62.0 (*C*H$_2$O), 120.1, 124.5 (aromatic *C*H), 126.4 (probably S*C*=), 129.0 (aromatic *C*H), 136.3, 137.3 (quaternary aromatic *C* and *C*Cl=), 164.4 (*C*O); Exact mass calculated for $C_{12}H_{14}ClNO_2S$ $[M]^+$ 271.04338. Found 271.04269; 271 (M^+, 9 %), 235

(15, M^+-HCl), 220 (28), 151 (40, M^+-CONHPh), 123 (52); isotopic Cl pattern observed; 271, 273 (3:1 ratio ^{35}Cl:^{37}Cl); *N*-phenyl-*Z*-2-[2′-(hydroxyethyl)thio]-2-butenamide **15h** (tentatively assigned as *Z*) (Rf 0.45) as a mixture with an unknown compound (*ca.* 70:30) (40 mg, 8% of total product mixture, estimated by ^1H NMR integration) as a yellow oil; δ_H 2.15 (3H, d, *J* 8, C*H*$_3$-4), 3.00 (2H, dd, *J* 7, 7, C*H*$_2$S), 3.64 (2H, dd, *J* 7, 7, C*H*$_2$O), 7.11-7.73 (6H, m, Ar*H* and C*H*=), 9.14 (1H, br s, N*H*); signals observed for the unknown compound at 2.44 (s), 3.09 (dd, *J* 7,7), 3.70 (dd, *J* 7, 7), 7.11-7.73 (m, ArH); *N*-phenyl-2-[2′-(hydroxyethyl)thio]-2,3,3-trichlorobutanamide **13h** (43 mg, 6 %) (Rf 0.35) as a yellow oil; ν_{max}/cm^{-1} (neat) 3394, 1686, 1599; δ_H 2.57 (3H, s, C*H*$_3$-4), 3.09, 3.11 (2H, 2 x dd, *J* 6, 6, C*H*$_A$*H*$_B$S), 3.83 (2H, dd, *J* 6, 6, C*H*$_2$O), 7.19 (1H, t, *J* 8, *H*-4′), 7.36 (2H, dd, *J* 8, 8, *H*-3′ and *H*-5′), 7.54 (2H, d, *J* 8 *H*-2′ and *H*-6′), 9.10 (1H, br s N*H*); δ_C 35.4, 36.5 (*C*H$_3$-4 and *C*H$_2$S), 60.0 (*C*H$_2$O), 92.1, 92.5 (*C*Cl$_2$-3 and *C*Cl-2), 120.5, 126.1, 129.2 (aromatic *C*H), 136.6 (quaternary aromatic *C*), 161.9 (*C*O); Exact mass calculated for $C_{12}H_{14}Cl_3NO_2S$ $[M]^+$ 340.98108. Found 340.98099; 341 (M^+, 1 %), 271 (1, M^+-2Cl), 120 (45), 93 (45), 77 (30, $[SCH_2CH_2OH]^+$); isotopic Cl pattern observed; 341, 343, 345, 347 (4:4:1:0.08 ratio $^{35}Cl^{37}Cl$); 271, 273 (3:1 ratio ^{35}Cl:^{37}Cl).

Use of amide substituent bearing a primary hydroxyl group

***N*-2′-[3′-Phenyl-1′-(2′′-chloropropoxylate)]propyl-2-chloropropanamide 19**

A solution of 2-chloropropanoyl chloride (3.45 g, 27.2 mmol) in DCM (20 ml) was added dropwise to a solution of (S)-phenylalaninol (2.01 g, 13.3 mmol) in DCM (50 ml) while stirring at RT. Stirring was continued for 16 h then saturated sodium bicarbonate (30 ml) was added. The phases were separated and the aqueous layer was extracted with DCM (2 x 10 ml). The combined organic layers were washed with water (2 x 10 ml), brine (2 x 10 ml), dried and evaporated to give the amide ester **19** (4.59 g, quantitative) as a white, crystalline solid which was used without further purification; mp 109-111 °C; ν_{max}/cm^{-1} (KBr) 3281, 1734, 1654, 1560; δ_H 1.59 (3H, d, *J* 7, C*H*$_3$CHCl), 1.65-1.70 (3H, m, C*H*$_3$CHCl), 2.89 (2H, br d, *J* 7, C*H*$_2$Ph), 4.10-4.47 (5H, m, OC*H*$_2$C*H*N, 2 x C*H*Cl), 6.77 (1H, br m, N*H*), 6.82-7.33 (5H, m, Ar*H*); δ_C 21.6, 22.6 (*C*H$_3$CHCl), 37.0 (*C*H$_2$Ph), 49.5,

52.3, 55.3 (3 x *C*H), 65.6 (*C*H_2O), 127.0, 128.4, 128.7 (Ar*C*H), 136.2 (quaternary aromatic *C*), 169.4, 169.8 (*C*O ester and *C*O amide); MS *m/z* 331 (M^+, 2%), 296 (1, M^+-Cl), 224 (75, M^+-$CH_3CHClCO_2$), 132 (100, $[CH_3CHClCO_2CH_2CH]^+$), isotopic Cl pattern observed; 331, 335, 337 (9:6:1 ratio ^{35}Cl,^{37}Cl), 132, 134 (3 :1 ratio ^{35}Cl,^{37}Cl).

(2R/S, 2′S)-*N*-2′-[(1′-hydroxy-3′-phenyl)propyl]-2-phenylthiopropanamide 10i

This was prepared following the procedure described for sulfide **10g** using **10i** (2.00 g, 6.04 mmol), thiophenol (1.3 ml, 12.7 mmol), sodium (0.57 g, 24.8 mmol) and dry ethanol (30 ml) to give the crude sulfide **10i** (1.90 g, 99 %). Ester hydrolysis took place during the washing of the organic phase with NaOH (5 M). Purification by recrystallisation from dry ethanol gave the sulfide **10i** (as an equimolar mixture of two diastereomers) (1.45 g, 76%), as a white, crystalline solid; mp 115-118 °C; Found C, 68.42; H, 6.89; N, 4.31; S, 10.15. $C_{18}H_{21}NO_2S$ requires C, 68.54; H, 6.71; N, 4.44; S, 10.17; ν_{max}/cm^{-1} (KBr) 3285, 1655; δ_H 1.41, 1.51 (3H, 2 x d, *J* 7, C*H*$_3$-3), 2.43 (1H, br s, O*H*), 2.74-2.86 (2H, m, C*H*$_2$Ph), 3.42-3.56 (2H, m, C*H*$_2$O), 3.74, 3.79 (1H, q, *J* 7, C*H*S), 4.02-4.18 (1H, br m, C*H*N), 6.85 (1H, br d, *J* 8, N*H*), 7.08-7.31 (10H, m, Ar*H*); δ_C 18.2, 18.4 (*C*H$_3$-3), 36.8, 36.9 (*C*H$_2$Ph), 47.1, 47.3 (*C*HS), 52.7, 53.2 (*C*HN), 63.9, 64.0 (*C*H$_2$O), 126.7, 127.6, 128.6, 129.3, 130.4 (aromatic *C*H), 134.1, 137.4 (quaternary aromatic *C*), 172.2, 172.6 (*C*O); MS *m/z* 315 (M^+, 30 %), 284 (10, M^+-CH_2OH), 224 (80, M^+-CH_2Ph), 137 (100, $[PhSCHCH_3]^+$), 91 (75, $[CH_2Ph]^+$).

(2′S)-2′-*N*-[1′-(Hydroxy)-3′-(phenyl)]propyl-*Z*-3-chloro-2-(phenylthio) propenamide 6i

A solution of **10i** (0.46 g, 1.46 mmol) in carbon tetrachloride (10 ml) was stirred at room temperature under nitrogen and NCS (0.40 g, 2.99 mmol) was added in one portion. The reaction mixture was then heated at reflux for 15 minutes. The reaction was cooled, filtered and concentrated to give **6i**. Purification by chromatography using ethyl acetate-methanol-hexane (30:5:65) as eluent gave β-chloroacrylamide **6i** (0.44 g, 86%) as a white, crystalline solid; mp 86-88 °C; $[\alpha]_D^{20}$ 95.9 (c 0.06 in EtOH); Found C, 62.23; H, 5.13; N, 3.80; S, 8.94. $C_{18}H_{18}ClNO_2S$ requires C, 62.15; H, 5.22; N, 4.03; S, 9.22;

ν_{max}/cm^{-1} (KBr) 3368, 1639, 1561; δ_H 2.23 (1H, br s, O*H*), 2.69-2.84 (2H, m, CH_2Ph), 3.34-3.55 (2H, m, CH_2O), 4.05-4.18 (1H, m, C*H*N), 7.05-7.41 (10H, m, Ar*H*), 7.85 (1H, s, C*H*Cl=); δ_C 37.6 (*C*H_2Ph), 54.1 (*C*HN), 64.3 (*C*H_2O), 127.6, 128.2, 129.4, 129.6, 130.1, 130.4 (aromatic *C*H), 131.8, 133.9, 138.0 (quaternary aromatic *C* and S*C*=), 140.0 (*C*HCl=), 163.5 (*C*O); MS *m/z* 347 (M^+, 8 %), 316 (6, M^+-CH_2OH), 256 (10, M^+-CH_2Ph), 166 (100), 134 (30, $[PhS=C=CH]^+$), 91 (70, $[CH_2Ph]^+$); isotopic Cl pattern observed; 347, 349 (3:1 ratio ^{35}Cl:^{37}Cl).

Synthesis of the Weinreb Amide derivatives

***N*-Methoxy-*N*-methyl-2-chloropropanamide 20**

The title compound was prepared as described previously[1] using N, O-dimethylhydroxylamine hydrochloride (5.00 g, 51.23 mmol), 2-chloropropionyl chloride (5.02 ml, 51.74 mmol) and triethylamine (15.60 ml, 112.71 mmol) in DCM (200 ml) for 4 hours. Following the work-up the amide **20** was isolated (7.30g, 76%) as a yellow oil which was used without further purification; δ_H 1.65 (3H, d, *J* 7, CH_3-3), 3.24 (3H, s, NCH_3), 3.79 (3H, s, OCH_3), 4.85-4.97 (1H, b q, C*H*Cl); δ_C 21.2 (*C*H_3-3), 32.9 (broad, N*C*H_3), 49.0 (O*C*H_3), 62.1 (*C*HCl), 170.2 (*C*O).

***N*-Methoxy-*N*-methyl-2-phenylthiopropanamide 10j**

The title compound was prepared as outlined for **10i** using *N*-methoxy-*N*-methyl-2-chloropropanamide **20** (5.00g, 33.00 mmol) and thiophenol (4.10 ml, 39.60 mmol) in freshly prepared sodium ethoxide [made from sodium (0.91 g, 39.60 mmol) and ethanol (80 ml) at 0^oC] for 18 h at room temperature. Following work-up as described previously, the sulfide **10j** was isolated (6.61 g, 89%) as a clear oil which was used without further purification. A sample (300 mg) was prepared for analysis by chromatography on silica gel using ethyl acetate-hexane (40:60) as eluent to give the sulfide (260 mg, 87% recovery) as a clear oil; Found C, 58.55; H, 6.90; N, 6.50; S, 14.47. $C_{11}H_{15}NO_2S$ requires C, 58.67; H, 6.67; N, 6.22; S, 14.22; δ_H 1.46 (3H, d, *J* 7, CH_3-3), 3.19 (3H, s, NCH_3), 3.64 (3H, s, OCH_3), 4.23-4.36 (1H, b q, C*H*S), 7.27-7.38 (3H, s, Ar*H*), 7.45-7.54 (2H, m, Ar*H*); δ_C 17.7 (*C*H_3-3), 32.5 (broad, N*C*H_3), 41.7 (O*C*H_3), 61.4 (*C*HS), 127.9 (aromatic *C*H), 128.5 (aromatic *C*H), 133.2 (quaternary aromatic), 133.5

(aromatic *C*H), 173.0 (*C*O); Exact mass calculated for $C_{11}H_{15}NO_2S$ $[M+]^+$ 225.0824. Found 225.0810; MS *m/z* 225 (M^+, 34%), 218 (18), 137 (100, M^+-$CONCH_3OCH_3$), 109 (45, $[SPh]^+$), 65 (15).

_N_-Methoxy-_N_-methyl-_Z_-3-chloro-2-phenylthiopropenamide _Z_-6j, _N_-Methoxy-_N_-methyl-_E_-3-chloro-2-phenylthiopropenamide _E_-6j, _N_-Methoxy-_N_-methyl-2,3-dichloro-2-phenylthiopropenamide 21j and _N_-Methoxy-_N_-methyl-2-phenylthiopropen-amide 15j

Note: Rotation about the C-N bond results in broadening of the ^{1}H NMR spectra of both isomers of the β-chloroacrylamides at 270MHz. This broadening is not seen when the ^{1}H NMR spectra are recorded at 60 MHz.

NCS (3.20 g, 23.99 mmol) was added to a solution of the sulfide **10j** (3.00 g, 13.33 mmol) in toluene (60 ml). The reaction solution was immediately lowered to a pre-heated oil bath at 120 °C. After heating for 2.5 h, the reaction solution was cooled to 0 °C and the succinimide by-product was removed by filtration. The toluene was removed by distillation at reduced pressure to give the crude β-chloroacrylamides in a ratio of 2:1. The crude reaction product was chromatographed on silica gel using ethyl acetate-hexane (20:80) as eluent to give the two β-chloroacrylamides, both as clear oils:

Major (less polar) β-chloroacrylamide **6j** (1.27 g, 37%), tentatively assigned as *Z*: Found C, 51.57; H, 4.71; N, 5.43; Cl, 13.80; S, 12.90. $C_{11}H_{12}NClO_2S$ requires C, 51.26; H, 4.69; N, 5.44; Cl, 13.75; S, 12.44; ν_{max}/cm^{-1} (film) 1661, 1581, 1475, 1440, 1382; δ_H (500MHz, 193K) 2.82 (1H, part of NC*H*$_3$ or NOC*H*$_3$), 3.08 (0.5H, part of NC*H*$_3$ or NOC*H*$_3$), 3.12 (0.5H, s, part of NC*H*$_3$ or NOC*H*$_3$), 3.19 (1.5H, s, part of NC*H*$_3$), 3.49 (0.5H, s, part of NOC*H*$_3$), 3.70 (2H, s, part of NOC*H*$_3$) 6.42 (0.28H, s, one rotamer of C*H*Cl=), 6.58 (0.72H, s, one rotamer of C*H*Cl=), 7.30-7.62 (5H, m, Ar*H*); δ_C (500MHz, 233K) 32.6 (part of N*C*H$_3$), 36.0 (part of N*C*H$_3$), 36.2 (part of N*C*H$_3$), 60.6 (part of NO*C*H$_3$), 61.1 (part of NO*C*H$_3$), 63.0 (part of NO*C*H$_3$), 119.9 (*C*HCl= of minor rotamer), 124.0 (*C*HCl= of major rotamer), 127-133 (aromatic signals for all rotamers), 135.2 (aromatic carbon), 135.5 (aromatic carbon), 158.2 (quaternary aromatic or C=O), 160.7 (quaternary aromatic or C=O), 163.6 (quaternary aromatic or C=O), 165.2 (quaternary aromatic or C=O); Exact mass calculated for $C_{11}H_{12}NClO_2S$ $[M+]^+$ 257.0277. Found

257.0278. MS *m/z* 257, 259 (M^+, 22), 222 (2, M^+-Cl), 197, 199 (17, M^+-NR_1R_2), 169, 171 (33, M^+-$CONR_1R_2$), 134 (100, $[PhS\text{-}C{=}CH]^+$), 109 (12, $[SPh]^+$); isotopic Cl pattern observed; 257, 259 (3:1 ratio of ^{35}Cl:^{37}Cl).

NMR spectra of this compound (^1H & ^{13}C) were also recorded in d_6-acetone: δ_H 3.16 (3H, s, NC*H*$_3$), 3.73 (3H, b s, OC*H*$_3$), 6.77 (1H, b s, C*H*Cl=), 7.28-7.62 (5H, m, Ar*H*); δ_C 32.4 (broad, N*C*H$_3$), 62.2 (broad, O*C*H$_3$), 123.3 (broad, aromatic *C*H), 130.1 (broad), 131.8 (broad), 133.8 (broad).

When the operating temperature of the ^1H NMR experiment was elevated (in $CDCl_3$), some sharpening of the signals was observed. This sharpening was at the optimum at 50^{o}C.

Minor (more polar) β-chloroacrylamide **6j** (0.93 g, 27%), tentatively assigned as *E*: Found C, 51.13; H, 4.86; N, 5.60; Cl, 13.64; S, 12.86. $C_{11}H_{12}NClO_2S$ requires C, 51.26; H, 4.69; N, 5.44; Cl, 13.75; S, 12.44; ν_{max}/cm^{-1} (film) 1659, 1474, 1440, 1378; δ_H (60 MHz) 2.82 (3H, s NC*H*$_3$), 3.46 (3H, s, OC*H*$_3$), 6.70 (1H, s, C*H*Cl=), 7.20-7.78 (5H, m, Ar*H*); Exact mass calculated for $C_{11}H_{12}NClO_2S$ $[M+]^+$ 257.0277. Found 257.0270. MS *m/z* 257, 259 (M^+, 34), 222 (2, M^+-Cl), 197, 199 (30, M^+-NR_1R_2), 169, 171 (29, M^+-$CONR_1R_2$), 134 (100, $[PhS\text{-}C{=}CH]^+$), 109 (13, $[SPh]^+$); isotopic Cl pattern observed; 257, 259 (3:1 ratio of ^{35}Cl:^{37}Cl).

The ^1H NMR spectrum of this compound was also recorded in d_6-acetone: δ_H 2.92 (3H, b s, NC*H*$_3$), 3.52 (3H, b s, OC*H*$_3$), 6.74 (1H, s, C*H*Cl=), 7.21-7.57 (5H, m, Ar*H*).

A fraction (500 mg) believed to be the dichloroacrylamide **21j** was also isolated; δ_H (60MHz) 3.27 (3H, s, NC*H*$_3$), 3.80 (3H, s, OC*H*$_3$), 7.28-7.80 (5H, m, Ar*H*).

Evidence for the acrylamide **15j** was also seen in the crude NMR spectrum at δ_H 5.36 (s) and 5.71 (s).

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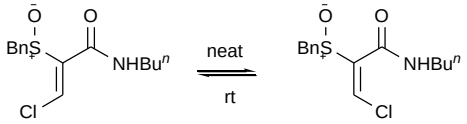

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