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<td><strong>Author(s)</strong></td>
<td>Kissane, Marie; Murphy, Maureen; Lynch, Denis; Ford, Alan; Maguire, Anita R.</td>
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Graphical Abstract

EWG=Ester, Nitrile, Amide,
X=Cl, Br
Investigation of the Reaction of \( \alpha \)-Thioamides, -esters and – nitriles with \( N \)-halosuccinimides

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Abstract

Investigation of the reaction of \( \alpha \)-thioamides, -esters and -nitriles with NBS and NCS is described. The scope of this stereoselective oxidative transformation to the \( \beta \)-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 \( \alpha \)-thioamides to the corresponding \( \alpha \)-thio-\( \beta \)-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.
Results and Discussion

Nitrile Derivatives

The reaction of the $\alpha$-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 $\beta$-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 $\alpha$-thioamides with NCS, with ZnCl$_2$ gave the corresponding $\beta$-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 $E$ $\beta$-chloroacrylonitriles 4 & 5 in a ratio of 6:1. Following chromatographic purification, a mixture of the $E$ and $Z$ $\beta$-chloroacrylonitriles was obtained as a yellow oil in the same ratio.

Thus, the methodology for the transformation of the amides to the corresponding $\beta$-chloroacrylamides is also applicable to the transformation of the $\alpha$-thionitrile to the corresponding $E$ and $Z$ $\beta$-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>
<thead>
<tr>
<th>Eq. NCS</th>
<th>Oil Bath Temp. (°C)</th>
<th>Time (h)</th>
<th>% 2†</th>
<th>% 3†</th>
<th>% 4,5†</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>130</td>
<td>18</td>
<td>20</td>
<td>80</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 1: Reaction of NCS with 1
After ZnCl$_2$ decomposition

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Temp (°C)</th>
<th>ZnCl$_2$</th>
<th>E</th>
<th>Z</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.95</td>
<td>130</td>
<td>18</td>
<td>40</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>2.1</td>
<td>130</td>
<td>48</td>
<td>66</td>
<td>33</td>
<td>&lt;5</td>
</tr>
<tr>
<td>2.1</td>
<td>130</td>
<td>48</td>
<td>-</td>
<td>&gt;90</td>
<td>-</td>
</tr>
<tr>
<td>2.1</td>
<td>160‡</td>
<td>18</td>
<td>Trace</td>
<td>Trace</td>
<td>-</td>
</tr>
<tr>
<td>1.95</td>
<td>140</td>
<td>18</td>
<td>73</td>
<td>9</td>
<td>18§</td>
</tr>
</tbody>
</table>

† 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.

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).
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

<table>
<thead>
<tr>
<th>Experiment†</th>
<th>R</th>
<th>% 14a</th>
<th>% 15a</th>
<th>% 11a</th>
<th>% 14c</th>
<th>% 15c</th>
<th>% 11c</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>OCH(_3)</td>
<td>70‡</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>OCH₃</td>
<td>&gt;90</td>
<td>Trace</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>---</td>
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<td>-------</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>NHTol</td>
<td>50</td>
<td>50</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>NHTol</td>
<td>-</td>
<td>33</td>
<td>66</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

†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 stabilization⁷ 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](image)

The decomposition of 11a & 11b to the corresponding β-chloroacrylates 6a & 6b was then achieved by reaction with 3 equivalents of ZnCl₂ 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 ZnCl₂ 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).

The preparation of the methanethio-substituted β-chloroacrylate 6e has also been attempted. When the α-thioester 10e 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 δH 4.85-5.05 with a coupling constant of 13 Hz in the ¹H NMR spectrum.

Although treatment of 11e with etheral ZnCl₂ affords a small amount of the desired acrylate (Scheme 3), unidentified decomposition products predominate in which loss of the methanethio signal was observed.
Preparation of Extended Chain β-Chloroacrylates

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

The mixed diastereomers of the crude dichloride 11f were treated with 3 equivalents of ZnCl₂ 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 ZnCl₂. It is likely that the ZnCl₂ 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 CDCl₃ when monitored by ¹H NMR spectroscopy over a prolonged period (Scheme 5). E-6g and Z-6g do not interconvert in the solid state.
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. 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 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.; the bromosulfonyl 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, 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 CCl₄ 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

<table>
<thead>
<tr>
<th>No. eq NBS</th>
<th>Temp (°C)</th>
<th>Solvent</th>
<th>Product Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0</td>
<td>0-20</td>
<td>CCl₄</td>
<td>No reaction</td>
</tr>
<tr>
<td>2.2</td>
<td>Reflux</td>
<td>CCl₄</td>
<td>1</td>
</tr>
<tr>
<td>2.2</td>
<td>Reflux</td>
<td>Toluene</td>
<td>1</td>
</tr>
</tbody>
</table>

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 CCl₄ 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 ¹H NMR spectrum of the crude product.

![Scheme 6](attachment://Scheme6.png)

As with the dichloro compounds, the most significant feature of the ¹H 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 δₗ 3.58 to 4.21 (J_AB 11) indicating the alteration in the environment of the CH₂ 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 ¹H NMR spectrum was seen at δₗ 7.93. Samples of 16a were stored at room temperature for up to 3 months with no evidence of any decomposition by ¹H NMR spectroscopy.

As with the chloro derivative 6a, only one isomer of the β-bromoacrylate 16a was evident on both ¹H and ¹³C 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.

![Chemical structures](image)

**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 with the sodium salt of mercaptoethanol (Scheme 7).

![Chemical reactions](image)

**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).

![Chemical reactions](image)

**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 $Z$ $\beta$-chloroacrylamides from $\alpha$-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 $E$ $\beta$-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 $\beta$-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 - $Z$-$\beta$-chloroacrylamide $Z$-6h (17%), $E$-$\beta$-chloroacrylamide $E$-6h (8%) and $E$ and $Z$ acrylamides 15h (12% combined).

![Scheme 9](image)

**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](image)

Treatment of the $\alpha$-thioamide 10i with 2.2 equivalents of NCS in CCl$_4$ under reflux conditions for 15 minutes gave the $Z$-$\beta$-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.\textsuperscript{17-19} The Weinreb amide \textit{20} was prepared as reported,\textsuperscript{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\textsuperscript{1} using thiophenol and sodium in ethanol for 18 hours. The α-thioamide \textit{10j} was obtained as a colourless oil in 87% yield (Scheme 11).

![Scheme 11]

The α-thioamide \textit{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 \textsuperscript{1}H NMR spectroscopy showed complete conversion of the sulfide to a mixture of the \textit{Z} and \textit{E} β-chloroacrylamides \textit{6j} in a ratio of 2:1. Some evidence for the acrylamide \textit{15j} was also observed in this spectrum. The \textit{E} and \textit{Z} isomers are separable by chromatography and were isolated in yields of 27\% and 37\% respectively. The dichloroacrylamide \textit{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 ZnCl₂. 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.

¹H (300 MHz) and ¹³C (75.5 MHz) NMR spectra were recorded on a Bruker (300 MHz) NMR spectrometer. ¹H (270 MHz) and ¹³C (67.8 MHz) NMR spectra were recorded on a Jeol GSX (270 MHz) NMR spectrometer. ¹H (60 MHz) NMR spectra were recorded on a Jeol PMX-60SI spectrometer. All spectra were recorded at room temperature (~20°C) in deuterated chloroform (CDCl₃) 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 PF254). 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 1H 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
ZnCl₂ (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; νmax/cm⁻¹ (film) 2230 (CN), 1551, 1478, 1442, 1146; δH 7.00 (0.86H, s,
CHCl= of one diastereomer), 7.14 (0.14H, s, CHCl= of one diastereomer), 7.35-7.59 (5H, m, ArH); δC 113.5 (CN of minor diastereomer), 115.9 (CN of major diastereomer), 128.5 (quaternary aromatic), 129.3 (aromatic CH), 129.8 (aromatic CH), 131.8 (CHCl= of minor diastereomer), 132.5 (CHCl= of major diastereomer), 134.3 (aromatic CH), 137.5 (SC= of minor diastereomer), 137.4 (SC= 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**  

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; νmax/cm−1 (film) 1753 (CO), 1440, 1286, 1258; δH 3.79 (3H, s, OCH3), 3.90-4.05 (2H, ABq, J 12, CH2Cl), 7.39-7.51 (3H, m, ArH), 7.65-7.71 (2H, m, ArH); δC 49.3 (CH2Cl), 53.9 (OCH3), 78.3 (SCCl), 128.0 (quaternary aromatic), 129.2 (aromatic CH), 131.2 (aromatic CH), 137.3 (aromatic CH), 166.0 (CO); Exact mass calculated for C10H10Cl2O2S [M]+ 263.9779. Found 263.9793; 264 [(M)+, 34%]. Evidence for the acrylate 15a was seen in some crude NMR spectra at δH 3.82 (s, OCH3), 5.24 (s, one of CH2) and 6.33 (s, one of CH2).

The NMR spectra of some crude reaction mixtures also showed evidence of the α-chloro sulfide 14a at δH 2.01 (s, CH3-3) and 3.72 (s, OCH3).

**Methyl 2-chloro-2-(phenylthio)propanoate 14a**  

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_1H 2.01 (3H, s, CH₃-3), 3.72 (3H, s, OCH₃), 7.21-7.62 (5H, m, ArH); 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°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_1H 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. C₁₁H₁₂Cl₂O₂S requires C, 47.32; H, 4.33; Cl, 25.40; S, 11.48. v_max/cm⁻¹ (film) 1747 (CO), 1441, 1256, 1185; δ_1H 1.29 (3H, t, J 7, CH₃), 3.82-4.01 (2H, ABq, J 12, CClH₂), 4.26 (2H, q, J 7, OCH₂), 7.33-7.52 (3H, m, ArH), 7.63-7.72 (2H, m, ArH); δ_C 13.8 (CH₂CH₃), 49.1 (CClH₂), 63.5 (OCH₂), 78.3 (SCCl), 127.5 (quaternary aromatic), 128.9 (aromatic CH), 131.0 (aromatic CH), 137.3 (aromatic CH), 165.4 (CO); Exact mass calculated for C₁₁H₁₂Cl₂O₂S [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-Cl₂), 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. ¹H 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 ZnCl₂ in ether (3 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. C₁₀H₉ClO₂S requires C, 52.52; H, 3.97; Cl, 15.50; S, 14.02. νmax/cm⁻¹ (film) 1732 (CO), 1557, 1271, 1242, 741; δH 3.67 (3H, s, OCH₃), 7.18-7.38 (5H, m, ArH), 7.71 (1H, s, CHCl=); δC 52.8 (OCH₃), 127.7 (aromatic CH), 129.3 (aromatic CH), 129.9 (aromatic CH), 133.3 (quaternary aromatic or SC=, one signal observed for 2 quaternary carbons), 138.0 (CHCl=), 163.7 (CO); MS m/z 228, 230 (M⁺, 100%), 192 (18, M⁺-HCl), 161 (35), 149 (42), 134 (100, [PhS-C=CH]⁺), 110 (48), 109 (42, [SPh]⁺); isotopic Cl pattern observed; 228, 230 (3:1 ³⁵Cl:³⁷Cl).

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 δH 3.72 (3H, s, OCH₃) and 6.76 (1H, s, CHCl₂-).

A further fraction (most polar, 25 mg) was also isolated and was shown to be the bis sulfide 12a with characteristic signals seen at δH 3.73 (3H, s, OCH₃), 7.18-7.58 (10H, m, ArH), 8.43 (1H, s, CHSPH=); Exact mass calculated for C₁₆H₁₄O₂S₂ [M⁺] 302.0435.
Found 302.0430; 302 (M^+, 100%), 193 (16, M^+-SPh), 161 (16), 134 (38, [PhS-C=CH]^+), 109 (17, [SPh]^+), 51 (12).

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

A solution of ZnCl₂ 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 ZnCl₂ 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. C₁₁H₁₁ClO₂S requires C, 54.43; H, 4.57; Cl, 14.61; S, 13.21. δmax/cm⁻¹ (film) 1728 (CO), 1560, 1267, 1242; δH 1.09 (3H, t, J 7, CH₃), 4.10 (2H, q, J 7, OCH₂), 7.20-7.51 (5H, m, ArH), 7.64 (1H, s, CHCl=); δC 13.7 (CH₂CH₃), 62.0 (OCH₂), 127.2 (aromatic CH), 128.7 (aromatic CH), 129.2 (aromatic CH), 130.1 (quaternary aromatic or S=C), 131.7 (quaternary aromatic or S=C), 136.9 (CHCl=), 163.2 (CO); 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-C=CH]^+), 109 (81, [SPh]^+), 77 (70); isotopic Cl pattern observed; 242, 244 (3:1 ^35Cl: ^37Cl).
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 ZnCl₂ (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. C₈H₁₃ClO₂S 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, C₃H₃-4'), 1.35-1.63 (4H, m, CH₂-3', CH₂-2'), 2.86 (2H, t, J 7, SCH₂), 3.83 (3H, s, OCH₃), 7.53 (1H, s, CHCl=); δ_C 13.8 (CH₃-4'), 21.9 (CH₂-3'), 32.2 (CH₂-2'), 33.2 (SCH₂), 53.1 (OCH₃), 136.2 (CHCl=). Quaternary carbons (SC= and CO) not observed; Exact mass calculated for C₈H₁₃ClO₂S [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 ³⁵Cl:²⁷Cl).

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%). \( \delta_H \) (300 MHz, CDCl\(_3\)) 5.07-4.95 (m, 2 H, CH\(_2\)), 3.87 (s, 3 H, OCH\(_3\)), 2.12 (s, 3 H, SCH\(_3\)).

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 chloroaicylate 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. \( \delta_H \) (300 MHz, CDCl\(_3\)) 3.83 (s, 3 H, OCH\(_3\)), 2.39 (s, 3 H, SCH\(_3\)).

**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; \( \delta_H \) 1.60 (1.8H, d, \( J_6 \), CH\(_3\) of major diastereomer), 1.84 (1.2H, d, \( J_6 \), CH\(_3\) of minor diastereomer), 3.58 (1.8H, s, OCH\(_3\) of major diastereomer), 3.60 (1.2H, s, OCH\(_3\) of minor diastereomer), 4.78-4.90 (1H, 2 overlapping q, CHCl-).

**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-chloroaicylate 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\(_2\)S requires C, 54.43; H, 4.57; Cl, 14.61; S, 13.21; \( \delta_H \) 2.43 (3H, s, =CCH\(_3\)), 3.49 (3H, s, OCH\(_3\)), 7.20-7.39 (5H, m, ArH); \( \delta_C \) 25.4 (CH\(_3\)), 52.4 (OCH\(_3\)), 127.5 (aromatic CH), 129.2 (aromatic CH), 130.8 (aromatic CH), 133.3 (quaternary aromatic or
SC= or CCl=), 136.7 (quaternary aromatic or SC= or CCl=), 143.5 (quaternary aromatic or SC= or CCl=), 165.2 (CO); MS m/z 242, 244 (M+, 20), 226 (30), 155 (43), 91 (46), 77 (100); isotopic Cl pattern observed; 242, 244 (3:1 35Cl:37Cl).

A second compound was also seen in the NMR, possibly the E isomer of the β-chloroacrylate, at δH 2.45 (3H, s, =CH3), 3.65 (3H, s, OCH3) and at δC 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; νmax/cm⁻¹ (neat) 3318 (br NH), 1676 (CO α,β-unsaturated amide); δH 2.31 (3 H, s, ArCH3), 7.07-7.47 (9 H, m, ArH), 8.31 (1 H, s, CHBr=); 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 79Br:81Br); N-4′-methylphenyl-3,3-dibromo-2-(phenylthio)propenamide 17c (10 mg) was also recovered as a colourless oil; νmax/cm⁻¹ (neat) 3298 (br NH), 1659, 1604 (CO amide); δH 2.27 (3 H, s, ArCH3), 7.03-7.65 (9 H, m, ArH); 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 79Br:81Br), 212, 214 (1:1 ratio 79Br:81Br).

**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 CCl₄ (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 ¹H NMR spectrum (60 MHz) was recorded (in CCl₄) 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. ¹H NMR spectroscopy (60 MHz in CCl₄) 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 ¹H NMR spectroscopy (60 MHz). The reaction solution was filtered to remove the succinimide by-product and the CCl₄ 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. C₁₀H₁₀Br₂O₂S requires C, 33.92; H, 2.85; Br, 45.14; S, 9.06. \[\text{wm}_{\text{CO}}/\text{cm}^{-1} (\text{film})\] 1747 (CO), 1439, 1269, 1165, 753; \[\delta_{\text{HH}} 3.58-3.63 (1H, \text{H}_A \text{ of ABq}, J 11, \text{one of CH}_2\text{Br}), 3.90 (3H, s, \text{OCH}_3), 4.16-4.21 (1H, \text{H}_B \text{ of ABq}, J 11, \text{one of CH}_2\text{Br}), 7.39-7.58 (3H, m, \text{ArH}), 7.74-7.82 (2H, m, \text{ArH}); \delta_{\text{CC}} 36.7 (\text{CH}_2\text{Br}), 54.1 (\text{OCH}_3), 69.3 (\text{SCBr}), 128.2 (\text{quaternary aromatic}), 129.0 (\text{aromatic CH}), 130.9 (\text{aromatic CH}), 137.0 (\text{aromatic CH}), 166.2 (CO); \text{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-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 \[\delta_{\text{HH}} 2.83 (s)\].

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

A solution of ZnCl₂ 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_{9}BrO_{2}S requires C, 43.97; H, 3.32;
Br, 29.25; S, 11.74.

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_{2}S 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, CH_{3}-3), 2.69-2.96 (3 H, m, CH_{2}S, OH),
3.63 (1 H, q, J 7, CH-2), 3.79-3.88 (2 H, m, CH_{2}O), 7.09-7.56 (5 H, m, ArH), 8.80 (1 H,
br s, NH); δ_{C} 18.4 (CH_{3}-3), 34.4 (CH_{2}S), 44.9 (CH-2), 61.8 (CH_{2}O), 120.0, 124.6, 129.1
(aromatic CH), 137.7 (quaternary aromatic C), 171.1 (CO); 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_{2}S requires C, 60.22; H, 7.16; N, 5.85; S, 13.40; \( \delta_{\text{H}} \) 1.06 (3H, t, J\( \text{CH}_3 \)=4), 1.70-1.84 (1H, m, CH\(_A\)H\(_B\)-3), 1.92-2.08 (1H, m, CH\(_A\)H\(_B\)-3), 2.68-2.88 (2H, m, CH\(_2\)S), 2.92-2.97 (1H, br t, O\( \text{H} \)), 3.45 (1H, t, J\( \text{JCH}_2\text{O} \)), 7.08-7.58 (5H, m, Ar\( \text{H} \)), 8.81 (1H, br s, NH); δ\(_C\) 12.0 (CH\(_3\)-4), 26.0 (CH\(_2\)-3), 34.5 (CH\(_2\)S), 52.3 (CH-2), 61.8 (CH\(_2\)O), 120.0, 124.6, 129.0 (aromatic CH), 137.7 (quaternary aromatic C), 170.2 (CO); MS \( m/\text{z} \) 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 \( \beta \)-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\(_2\)S requires C, 51.26; H, 4.69; N, 5.43; \( \nu_{\text{max}}/\text{cm}^{-1} \) (neat) 3336, 1668, 1598; δ\(_H\) H\(_2\)O peak seen at 1.70-1.90 (br s), 2.56 (1H, s, O\( \text{H} \)), 3.15 (2H, t, J\( \text{JCH}_2\text{S} \)), 3.67 (2H, t, J\( \text{JCH}_2\text{O} \)), 7.14-7.66 (5H, m, Ar\( \text{H} \)), 7.97 (1H, s, CHCl\(=\)), 9.08 (1H, br s, NH); δ\(_C\) 36.7 (CH\(_2\)S), 42.7 (CH\(_2\)O), 120.2, 125.1, 129.2 (aromatic CH and SC\(=\)), 130.9, 137.2 (quaternary aromatic C), 140.7 (CHCl\(=\)), 160.6 (CO); MS \( m/\text{z} \) 275 (M\(^+\) + H\(_2\)O, 8 %), 240 (10, M\(^+\) + H\(_2\)O -Cl), 163 (100, M\(^+\) +H\(_2\)O -[S(CH\(_2\)\(_2\)OH]\(^+\)); isotopic Cl pattern observed; 275, 277 (3:1 ratio \(^{35}\text{Cl} :^{37}\text{Cl}\) and \( \beta \)-chloroacrylamide 6g (tentatively assigned as Z) (1.14...
g, 33 %) (Rf 0.1) as a colourless oil; δH 2.56 (1H, br s, OH), 2.99 (2H, t, J 6, CH2S), 3.79 (2H, t, J 6, CH2O), 7.12-7.64 (5H, m, ArH), 7.85 (1H, s, CHCl=). 9.33 (1H,br s, NH); δC 37.2 (CH2S), 60.4 (CH2O), 120.2, 125.0, 129.0 (aromatic CH), 131.7, 137.3 (quaternary aromatic C and SC=), 139.6 (CHCl=), 161.4 (CO); Exact mass calculated for C11H12ClNO2S [M]+ 257.02773. Found 257.02451; 257 (M+ ,18 %), 239 (18, M+ -Cl), 204 (58), 178 (43), 93 (100, [NH2Ph]+), isotopic Cl pattern observed; 257, 259 (3:1 ratio 35Cl:37Cl).

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; νmax/cm−1 (neat) 3278, 1651, 1598; δH 2.48 (3H, s, CH3-4), 2.94 (2H, dd, J 5, 5, CH2S), 3.80 (2H, dd, J 5, 5, CH2O), 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, NH); δC 25.5 (CH3-4), 36.6 (CH2S), 61.1 (CH2O), 119.9, 124.9 (aromatic CH), 126.7 (probably SC=), 129.1 (aromatic CH), 137.5 (quaternary aromatic C), 144.5 (CCl=), 163.6 (CO); Exact mass calculated for C12H14ClNO2S [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 35Cl:37Cl); 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; δH 2.42 (3H, s, CH3-4), 2.91 (2H , dd, J 5, 5, CH2S), 3.10-3.50 (1H, br s, OH), 3.84 (2H, dd, J 5, 5, CH2O), 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, NH); δC 24.2 (CH3-4), 37.0 (CH2S), 62.0 (CH2O), 120.1, 124.5 (aromatic CH), 126.4 (probably SC=), 129.0 (aromatic CH), 136.3, 137.3 (quaternary aromatic C and CCl=), 164.4 (CO); Exact mass calculated for C12H14ClNO2S [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 ⁢₃⁵Cl: ⁢₃⁷Cl); 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; δH 2.15 (3H, d, J 8, CH₃-4), 3.00 (2H, dd, J 7, 7, CH₂S), 3.64 (2H, dd, J 7, 7, CH₂O), 7.11-7.73 (6H, m, ArH and CH=), 9.14 (1H, br s, NH); 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; v_max/cm⁻¹ (neat) 3394, 1686, 1599; δH 2.57 (3H, s, CH₃-4), 3.09, 3.11 (2H, 2 x dd, J 6, 6, CH₂H₃S), 3.83 (2H, dd, J 6, 6, CH₂O), 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 NH); δC 35.4, 36.5 (CH₃-4 and CH₂S), 60.0 (CH₂O), 92.1, 92.5 (CCl₂-3 and CCl-2), 120.5, 126.1, 129.2 (aromatic CH), 136.6 (quaternary aromatic C), 161.9 (CO); Exact mass calculated for C₁₂H₁₄Cl₃NO₂S [M⁺] 340.98108. Found 340.98099; 341 (M⁺, 1%), 271 (1, M⁺-2Cl), 120 (45), 93 (45), 77 (30, [SCH₂CH₂OH]+); isotopic Cl pattern observed; 341, 343, 345, 347 (4:4:1:0.08 ratio ⁢₃⁵Cl: ⁢₃⁷Cl); 271, 273 (3:1 ratio ⁢₃⁵Cl: ⁢₃⁷Cl).

Use of amide substituent bearing a primary hydroxy 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; v_max/cm⁻¹ (KBr) 3281, 1734, 1654, 1560; δH 1.59 (3H, d, J 7, CH₃CHCl), 1.65-1.70 (3H, m, CH₃CHCl), 2.89 (2H, br d, J 7, CH₂Ph), 4.10-4.47 (5H, m, OCH₂CHN, 2 x CHCl), 6.77 (1H, br m, NH), 6.82-7.33 (5H, m, ArH); δC 21.6, 22.6 (CH₃CHCl), 37.0 (CH₂Ph), 49.5,
52.3, 55.3 (3 x CH), 65.6 (CH₂O), 127.0, 128.4, 128.7 (ArCH), 136.2 (quaternary aromatic C), 169.4, 169.8 (CO ester and CO amide); MS m/z 331 (M⁺, 2%), 296 (1, M⁺-Cl), 224 (75, M⁺-CH₃CHClCO₂), 132 (100, [CH₃CHClCO₂CH₂CH]⁺), isotopic Cl pattern observed; 331, 335, 337 (9:6:1 ratio ³⁵Cl, ³⁷Cl), 132, 134 (3 :1 ratio ³⁵Cl, ³⁷Cl).

(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 ºC; Found C, 68.42; H, 6.89; N, 4.31; S, 10.15. C₁₈H₂₁NO₂S requires C, 68.54; H, 6.71; N, 4.44; S, 10.17; ν max/cm⁻¹ (KBr) 3285, 1655; δH 1.41, 1.51 (3H, 2 x d, J 7, CH₃-3), 2.43 (1H, br s, OH), 2.74-2.86 (2H, m, CH₂Ph), 3.42-3.56 (2H, m, CH₂O), 3.74, 3.79 (1H, q, J 7, CHS), 4.02-4.18 (1H, br m, CHN), 6.85 (1H, br d, J 8, NH), 7.08-7.31 (10H, m, ArH); δC 18.2, 18.4 (CH₃-3), 36.8, 36.9 (CH₂Ph), 47.1, 47.3 (CHS), 52.7, 53.2 (CHN), 63.9, 64.0 (CH₂O), 126.7, 127.6, 128.6, 129.3, 130.4 (aromatic CH), 134.1, 137.4 (quaternary aromatic C), 172.2, 172.6 (CO); MS m/z 315 (M⁺, 30 %), 284 (10, M⁺-CH₂OH), 224 (80, M⁺-CH₂Ph), 137 (100, [PhSCHCH₃]⁺), 91 (75, [CH₂Ph]⁺).

(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 ºC; [α] D{eq}^{20}_{20} 95.9 (c 0.06 in EtOH); Found C, 62.23; H, 5.13; N, 3.80; S, 8.94. C₁₈H₁₈ClNO₂S requires C, 62.15; H, 5.22; N, 4.03; S, 9.22;
\[ \nu_{\text{max}}/\text{cm}^{-1} \] (KBr) 3368, 1639, 1561; \( \delta_H \) 2.23 (1H, br s, OH), 2.69-2.84 (2H, m, CH\(_2\)Ph), 3.34-3.55 (2H, m, CH\(_2\)O), 4.05-4.18 (1H, m, CHN), 7.05-7.41 (10H, m, ArH), 7.85 (1H, s, CHCl=); \( \delta_C \) 37.6 (CH\(_2\)Ph), 54.1 (CHN), 64.3 (CH\(_2\)O), 127.6, 128.2, 129.4, 129.6, 130.1, 130.4 (aromatic CH), 131.8, 133.9, 138.0 (quaternary aromatic and SC=), 140.0 (CHCl=), 163.5 (CO); MS \( m/z \) 347 (M\(^+\), 8%), 316 (6, M\(^+\)-CH\(_2\)OH), 256 (10, M\(^+\)-CH\(_2\)Ph), 166 (100), 134 (30, [PhS=\( C=\text{CH}\)]\(^+\)), 91 (70, [CH\(_2\)Ph]+); isotopic Cl pattern observed; 347, 349 (3:1 ratio \(^{35}\text{Cl}:^{37}\text{Cl}\)).

**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 (7.30 g, 76%) as a yellow oil which was used without further purification; \( \delta_H \) 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, CHCl); \( \delta_C \) 21.2 (CH\(_3\)-3), 32.9 (broad, NCH\(_3\)), 49.0 (OCH\(_3\)), 62.1 (CHCl), 170.2 (CO).

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

The title compound was prepared as outlined for 10i using N-methoxy-N-methyl-2-chloropropanamide 20 (5.00 g, 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°C] 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\(_2\)S requires C, 58.67; H, 6.67; N, 6.22; S, 14.22; \( \delta_H \) 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, CHS), 7.27-7.38 (3H, s, ArH), 7.45-7.54 (2H, m, ArH); \( \delta_C \) 17.7 (CH\(_3\)-3), 32.5 (broad, NCH\(_3\)), 41.7 (OCH\(_3\)), 61.4 (CHS), 127.9 (aromatic CH), 128.5 (aromatic CH), 133.2 (quaternary aromatic), 133.5
(aromatic CH), 173.0 (CO); Exact mass calculated for C₁₁H₁₅NO₂S [M+]⁺ 225.0824. Found 225.0810; MS m/z 225 (M⁺, 34%), 218 (18), 137 (100, M⁺-CONCH₃OCH₃), 109 (45, [SPh⁺]), 65 (15).


Note: Rotation about the C-N bond results in broadening of the ¹H NMR spectra of both isomers of the β-chloroacrylamides at 270MHz. This broadening is not seen when the ¹H 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. C₁₁H₁₂NClO₂S 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 NCH₃ or NOCH₃), 3.08 (0.5H, part of NCH₃ or NOCH₃), 3.12 (0.5H, s, part of NCH₃ or NOCH₃), 3.19 (1.5H, s, part of NCH₃), 3.49 (0.5H, s, part of NOCH₃), 3.70 (2H, s, part of NOCH₃) 6.42 (0.28H, s, one rotamer of CHCl=), 6.58 (0.72H, s, one rotamer of CHCl=), 7.30-7.62 (5H, m, ArH); δ_C (500MHz, 233K) 32.6 (part of NCH₃), 36.0 (part of NCH₃), 63.0 (part of NOCH₃), 119.9 (CHCl= of minor rotamer), 124.0 (CHCl= 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 C₁₁H₁₂NClO₂S [M+]⁺ 257.0277. Found
257.0278. MS m/z 257, 259 (M+, 22), 222 (2, M+-Cl), 197, 199 (17, M+-NR1R2), 169, 171 (33, M+-CONR1R2), 134 (100, [PhS-C=CH]+), 109 (12, [SPh]+); isotopic Cl pattern observed; 257, 259 (3:1 ratio of $^{35}$Cl:$^{37}$Cl).

NMR spectra of this compound ("H & "C) were also recorded in d$_6$-acetone: $\delta_H$ 3.16 (3H, s, NCH$_3$), 3.73 (3H, b s, OCH$_3$), 6.77 (1H, b s, CHCl=), 7.28-7.62 (5H, m, ArH); $\delta_C$ 32.4 (broad, NCH$_3$), 62.2 (broad, OCH$_3$), 123.3 (broad, aromatic CH), 130.1 (broad), 131.8 (broad), 133.8 (broad).

When the operating temperature of the $^1$H NMR experiment was elevated (in CDCl$_3$), some sharpening of the signals was observed. This sharpening was at the optimum at 50°C.

Minor (more polar) $\beta$-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$_2$S requires C, 51.26; H, 4.69; N, 5.44; Cl, 13.75; S, 12.44; $\nu$$_{max}$/cm$^{-1}$ (film) 1659, 1474, 1440, 1378; $\delta_H$ (60 MHz) 2.82 (3H, s NCH$_3$), 3.46 (3H, s, OCH$_3$), 6.70 (1H, s, CHCl=), 7.20-7.78 (5H, m, ArH); Exact mass calculated for C$_{11}$H$_{12}$NClO$_2$S [M+]$^+$ 257.0277. Found 257.0270. MS m/z 257, 259 (M+, 34), 222 (2, M+-Cl), 197, 199 (30, M+-NR1R2), 169, 171 (29, M+-CONR1R2), 134 (100, [PhS-C=CH]+), 109 (13, [SPh]+); isotopic Cl pattern observed; 257, 259 (3:1 ratio of $^{35}$Cl:$^{37}$Cl).

The $^1$H NMR spectrum of this compound was also recorded in d$_6$-acetone: $\delta_H$ 2.92 (3H, b s, NCH$_3$), 3.52 (3H, b s, OCH$_3$), 6.74 (1H, s, CHCl=), 7.21-7.57 (5H, m, ArH).

A fraction (500 mg) believed to be the dichloroacrylamide 21j was also isolated; $\delta_H$ (60MHz) 3.27 (3H, s NCH$_3$), 3.80 (3H, s, OCH$_3$), 7.28-7.80 (5H, m, ArH).

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

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**References**


10. A similar effect has been observed for the benzylsulfinyl derivative $N$-$n$-butyl-Z-3-chloro-2-(benzylsulfinyl)propenamide, which is an oil at room temperature. When left at room temperature for a period of time, the $Z$ isomer was seen to interconvert to the $E$ isomer.


