A General Synthesis of *N*-Substituted Isothiazol-3(2*H*)-ones

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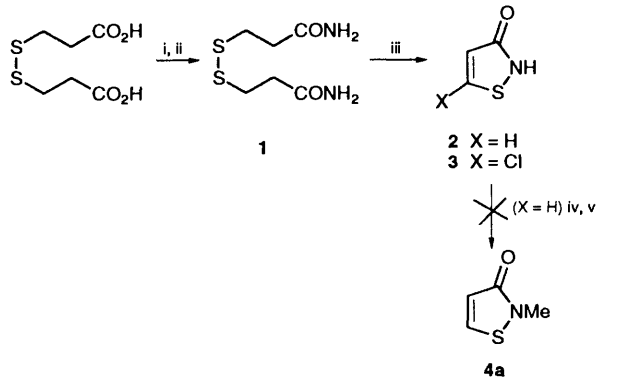
A general route to the synthesis of *N*-substituted isothiazol-3(2*H*)-ones (**4a–i**) is described which proceeds *via* trichloroacetic acid-mediated ring closure of *N*-substituted (*Z*)-3-(benzylsulfinyl)propenamides (**15a–i**).

Isothiazol-3(2*H*)-ones have found a range of industrial applications and are widely used as antimicrobial and algicidal additives.[1] One of the earliest synthetic isothiazole derivatives to be prepared was benzoisothiazol-3(2*H*)-one 1,1-dioxide, better known as saccharin, which was prepared by Remsen and Fahlberg in 1879.[2] However, it was more than three quarters of a century later before Adams and Slack[3] synthesised the parent isothiazole by a degradative route starting with 5-aminobenzoisothiazole and it was not until the early 1960s that any practical routes to these systems and their derivatives were devised.

Cyclisation of γ-imino thiols or their tautomers may be achieved with oxidants such as halogens, hydrogen peroxide, peroxy acids or high potential quinones.[4] The route has general applicability, with few constraints on the substituents present, but the main drawback is the difficulty of access to the acyclic precursors. An improved method designed specifically for the formation of isothiazol-3(2*H*)-ones was described by Lewis,[5] in which the key step involves the oxidative annelation of 3,3'-disulfanediyldipropanamides using either chlorine or sulfuryl chloride as oxidant. In 1962 Wille[6] developed an extremely convenient method of forming isothiazoles by controlled cyclisation of the *Z*-isomer of *N*-sulfanylacrylamide obtained from the reaction between propynal and sodium thiosulfate or thiocyanate. An improved variant employs potassium thiohydroxylamino-*S*-sulfate.[7] Crow and Leonard[8] extended the methodology to synthesise the first examples of unsubstituted isothiazol-3(2*H*)-ones. In 1963 Hatchard[9] described the synthesis of the disodium salt of 4-cyano-3-hydroxy-5-thioisothiazole by the oxidative cyclisation of disodium dicyanomethylenemalonate, itself obtained from the reaction of malononitrile with carbon disulfide under basic conditions.

In connection with our interest in the construction of novel polycyclic systems *via* Diels–Alder reactions, we required ready access to a range of *N*-alkylated isothiazol-3(2*H*)-ones. Of the methods described above, that of Lewis was initially considered most suitable for our needs and thus 3,3'-disulfanediyldipropanamide **1** was prepared by allowing concentrated aqueous ammonium hydroxide to react with the bis(acid chloride) in the presence of a catalytic quantity of pyridine. However, attempted cyclisation with chlorine led to recovery of the initial amide under a range of conditions. Repeating the cyclisation using sulfuryl chloride as oxidant furnished only 10% of the desired isothiazol-3(2*H*)-one **2** (R = H) having physical and spectroscopic data consistent with the literature values (Scheme 1).[5] A modified method described by Abou-Gharbia,[10] in which the amide is refluxed with sulfuryl chloride, did not improve the yield and also generated 4-chloroisothiazol-3(2*H*)-one **3** in 18% yield. Nevertheless, with some quantity of the parent isothiazol-3(2*H*)-one available, *N*-methylation was attempted under a variety of conditions, all of which failed to furnish the desired material **4a**, furnishing either starting material or decomposition products under more forcing conditions. This may be a result of alkylation occurring



Scheme 1 *Reagents and conditions:* i, $SOCl_2$, py; ii, aq. NH_3; iii, SO_2Cl_2, CH_2Cl_2, reflux (X = H, Cl); iv, (X = H) KOH, NaH, or KH, THF; v, MeI

preferentially on oxygen due to the quasi-aromatic nature of the anion formed on deprotonation of the parent isothiazol-3(2*H*)-one **2**.

Attempts at direct synthesis of the *N*-alkylated isothiazol-3(2*H*)-ones by cyclising secondary amide derivatives with sulfuryl chloride in the above route likewise gave only low yields of the desired products, contaminated by appreciable quantities of the 5-chlorinated products. Employing the conditions of Abou-Gharbia *et al.* had the effect of improving the yield of desired isothiazol-3(2*H*)-ones, but these were always contaminated with appreciable quantities of 5-chloroisothiazol-3(2*H*)-ones.[10]

In a recent paper by Wright,[11] cyclisation of sulfoxide substrates acting as sulfanyl halide equivalents has been described. In the case of the benzyl sulfoxide **5a**, cyclisation was mediated by trichloroacetic anhydride; whereas the *tert*-butyl sulfoxide **5b** cyclised under thermal conditions, with concomitant loss of isobutene, yielding the benzoisothiazolones **6**. Minor quantities of by-products **7**, resulting from a Pummerer rearrangement pathway were also observed (Scheme 2).

In the light of the difficulties we had experienced with the previous routes, we decided to attempt to adapt this approach to the preparation of non-benzannulated analogues. Following the procedure of Haefliger and Petrzilka,[12] toluene-α-thiol and propynoic acid were refluxed in ethanolic sodium carbonate to give (*Z*)-3-(benzylsulfanyl)propenoic acid in 85% yield (Scheme 3). Truce has shown that the addition of thiols to alkynes furnishes preferentially *Z*-adducts under base-catalysed conditions, whilst the equivalent non-catalysed system yields *E*-sulfides.[13] With the acid **8** in hand, the next objective was to find an efficient method of generating the range of amides required for the study. Initial investigations using *N*,*N*'-dicyclohexylcarbodiimide coupling[14] failed to give any expected amide products and resulted in poor recovery of

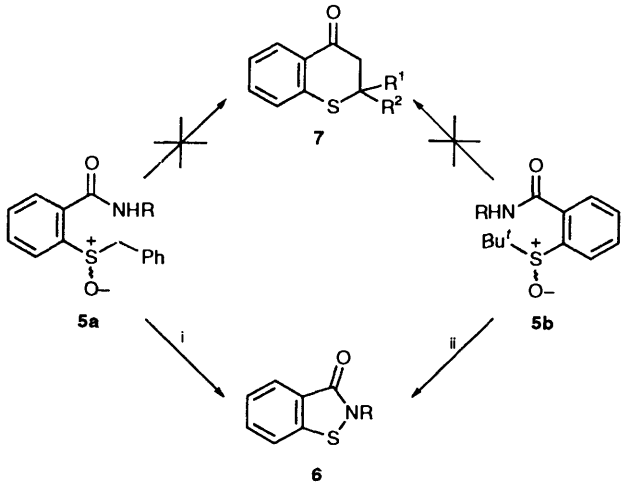
starting acid with ureide formation dominating. The activated esters **9** and **10** derived from 4-nitrophenol[15] and *N*-hydroxysuccinimide,[16] respectively, were also investigated, but only low yields of coupling products were obtained with these substrates. The use of mixed anhydrides was also disappointing. Following the method of Vaughan,[17] isobutyl chloroformate was allowed to react with the alkenoic acid in the presence of triethylamine at −15 °C, followed by the addition of the requisite amine and warming to room temperature. In all cases, except when methylamine was used, only starting materials were isolated. The 1-(3-benzylsulfanyl-*Z*-propenoyl)imidazole **11** was successfully prepared in 80% yield as a crystalline solid but, once again, reaction with isopropylamine failed to give the desired amide.

Success was eventually achieved by activating the (*Z*)-3-benzylsulfanylpropenoic acid **8** with diphenylphosphinic chloride to furnish the phosphinic ester **12** which was not isolated, but allowed to react directly with a range of amines.[18] Using this approach efficient coupling was carried out with a range of aliphatic and aromatic amines (Table 1). Comparison of the NMR spectrum of the methyl amide **14a** with that of the parent acid **8** showed a shift in the vinylic protons from δ 7.21 and 5.85 ppm for **8** to δ 6.79 and 5.72 ppm for **14a**. This greater upfield shift of the lower field of the two vinylic signals compared to the starting acid was a characteristic feature in the NMR spectra of all the amides prepared.

However, 4-nitroaniline and ethyl 4-aminobenzoate, showed no reaction, even after extended reaction times, presumably due to the relatively poor nucleophilicity of these amines. These two amines could be successfully coupled by reaction at −20 °C with (*Z*)-3-benzylsulfanylpropenoyl chloride **13** prepared *in situ* with oxalyl chloride, although the procedure was much less convenient than that proceeding *via* the phosphinate derivative. If the temperature was not maintained at −20 °C, *E*-isomerised by-products were formed.

In all instances the amides **14a–j** were converted smoothly into the corresponding sulfoxides **15a–j** with 3-chloroperbenzoic acid in dichloromethane at −20 °C (see also Table 1). Analysis of the NMR spectra of the products showed a characteristic two-proton AB quartet due to the diastereotopic benzylic methylene protons α to the sulfoxide. In the case of the nitro amide **14j**, the sulfoxide **15j** was precipitated from the reaction mixture as it was formed, thus simplifying purification.

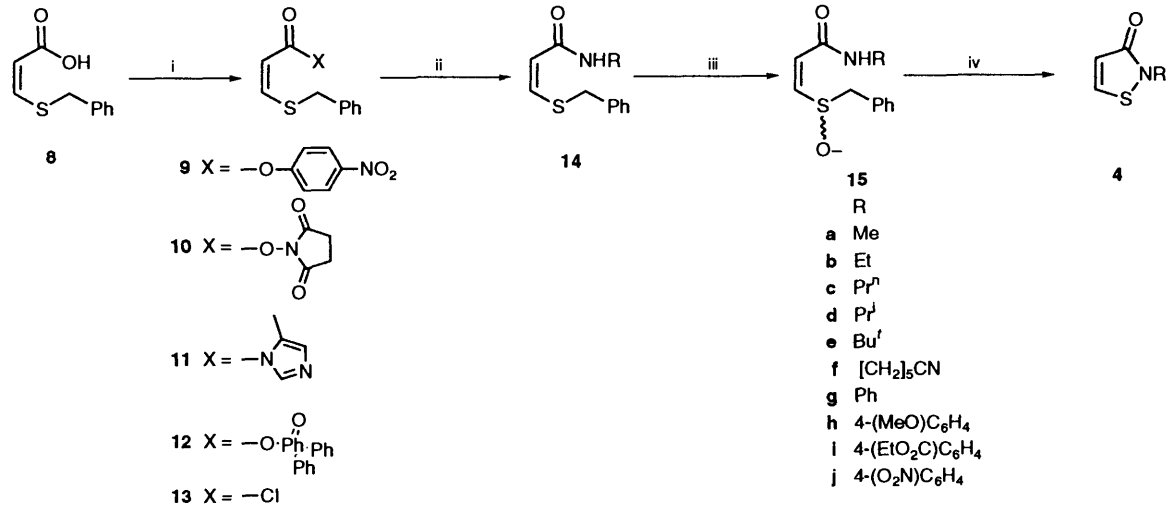
Cyclisation of the sulfoxides in dichloromethane at 0 °C using trichloroacetic anhydride furnished the corresponding *N*-alkylisothiazol-3(2*H*)-ones **4a–i** in good yield after chromatographic separation from the benzyl trichloroacetate formed during reaction (Table 1). An exception was (*Z*)-*N*-3-(benzylsulfinyl)-



Scheme 2 *Reagents and conditions:* i, $(Cl_3CO)_2O$, CH_2Cl_2, 0 °C; ii, py, toluene, reflux R = aryl, R^1 = H, Me, R^2 = Me, Ph

Table 1 Reaction of the phosphinic ester **12** with aliphatic and aromatic amines to give the amides **14a–j**, sulfoxides **15a–j** and isothiazol-3(2*H*)-ones **4a–i**

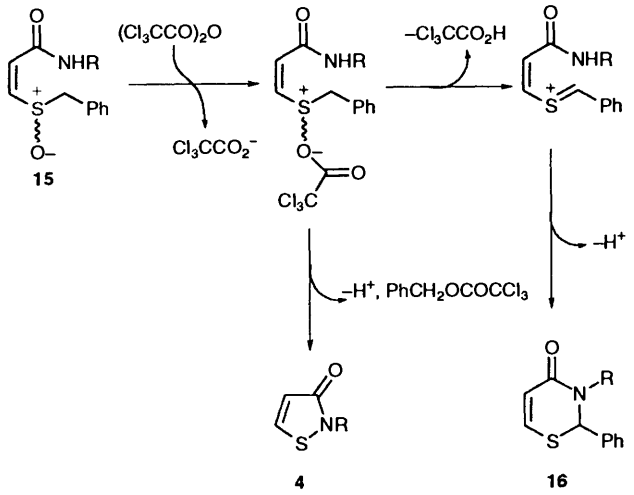
	R	Isolated yield (%) 14	15	4
a	Me	71	69	66
b	Et	69	89	68
c	Pr	58	87	62
d	Pr^i	82	90	67
e	Bu^t	85	74	41
f	$[CH_2]_5CN$	62	87	48
g	Ph	62	90	74
h	4-$(MeO)C_6H_4$	83	69	65
i	4-$(EtO_2C)C_6H_4$	69	91	42
j	4-$(O_2N)C_6H_4$	62	96	0



Scheme 3 *Reagents and conditions:* i, 4-$(O_2N)C_6H_4OH$, DCCI, THF (X = $OC_6H_4NO_2$-4); *N*-hydroxysuccinimide, DCCI, THF [X = O-(*N*-succinimidyl)]; 1,1′-carbonyldimidazole, THF (X = imidazol-1-yl); Ph_2POCl, THF, *N*-Methylmorpholine, −10 °C, 1 h; [X = $O(PO)Ph_2$], $(COCl)_2$, CH_2Cl_2, DMF (cat.) (X = Cl); ii, [X = $O(PO)Ph_2$, R = Me, Et, Pr, Pr^i, Bu^t, C_5H_8CN, Ph, 4-$(MeO)C_6H_4$; X = Cl, R = 4-$(EtO_2C)C_6H_4$, 4-$(O_2N)C_6H_4$], RNH_2, THF, −20 °C–RT; iii, MCPBA, CH_2Cl_2 or THF, −20 °C; iv, $(Cl_3CO)_2O$, CH_2Cl_2 or DMF, 0 °C–RT

(4-nitrophenyl)propenamide **15j**, which proved to be insoluble in dichloromethane and did not undergo cyclisation in those solvents (*e.g.* DMF) in which it was soluble.

A mechanistic sequence for isothiazol-3(2*H*)-one ring formation using trichloroacetic anhydride is shown in Scheme 4.



Scheme 4

No signals which might correspond to Pummerer rearrangement products **16** could be detected in the NMR spectrum of the crude reaction mixture nor could any material other than the isothiazol-3(2*H*)-ones be isolated. It appears, therefore, that initial electrophilic attack of the trichloracetic anhydride on the sulfoxide oxygen is largely followed by cyclisation of the sulfonium species and elimination of trichloroacetic acid does not constitute a major pathway.

It is impossible to rule out the possibility of hydrolytic decomposition of the products of Pummerer rearrangement but, even if this rearrangement pathway operates, it represents a relatively minor diversion from the main cyclisation pathway. However, it is worthy of note that Wright found that the corresponding cyclisations in the benzannelated systems gave approximately 5% of Pummerer rearrangement products (see Scheme 2).[11] Repeating the cyclisations with the *N*-methyl **15a**, *N*-isopropyl **15d** and *N*-4-methoxyphenyl **15h** sulfoxides using trifluoroacetic anhydride instead of trichloroacetic anhydride led to a decline in yields of the isothiazol-3(2*H*)-ones isolated (**4a** 30%, **4d** 25% and **4h** 40%) but, as before, no Pummerer product was identified nor starting material recovered. This result does provide circumstantial evidence for increased operation of the Pummerer rearrangement pathway, with subsequent hydrolytic decomposition of the products on work-up. In support of the key cyclisation step involving intramolecular nucleophilic attack on the sulfur, it was observed that an electron-rich aromatic substituent on the nitrogen led to improved yields of cyclisation with sulfoxide **15h**. Conversely, electron-deficient substituents hindered reaction, with the *N*-(4-ethoxycarbonylphenyl) substrate **15i** cyclising in only 42% yield (Table 1, entry 9) and the *N*-(4-nitrophenyl) substrate **15j** proving unreactive.

Despite the failure in the case of *N*-(4-nitrophenyl) substrate **15j**, the approach to isothiazol-3(2*H*)-ones described in this paper has been shown to be versatile and capable of tolerating a wide range of *N*-substitution, with the only limitation appearing to be strongly mesomerically electron-withdrawing substituents. The sequence is experimentally simple to carry out, gives consistently good overall yields and is tolerant of steric bulk at the nitrogen. The isothiazol-3(2*H*)-ones thus produced are easily purified by chromatography or recrystallisation.

Experimental

General Procedures.—Melting points (uncorrected) were recorded on a Kofler hot-stage apparatus. Microanalyses were carried out on a Carlo Erba 1106 elemental analyser. IR spectra were recorded on a Perkin-Elmer 1750 FT spectrometer. ^{1}H NMR spectra were recorded on Varian Gemini 200 (200 MHz), Bruker AC200 (200 MHz) and Bruker AM500 (500 MHz) spectrometers in $CDCl_3$, CD_3OD or $(CD_3)_2SO$ as stated and were referenced to residual protons [$CHCl_3$, δ_H 7.27; CH_3OH, δ_H 3.31; $(CH_3)_2SO$, δ_H 2.50]. The signals were assigned according to the following multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, sept = septet and m = multiplet, with br denoting a broadened signal. Mass spectra were recorded on V.G. Masslab 20-250, V.G. Micromass 30F, ZAB 1F or Trio-1 GC-MS (DB-5 column) spectrometers, using chemical ionisation (CI) with ammonia as the ionising source; *m/z* values are followed by their percentage abundance in parentheses. Thin layer chromatography (TLC) was performed on Merck DC-Plastikfolien or DC-Alufolien TLC plates coated with silica $60F_{254}$. Plates were visualised by UV light, by staining with I_2, or by charring with ceric sulfate–ammonium molybdate in 5% aqueous sulfuric acid, a 0.3 mol dm^{-3} solution of vanillin in acidic methanol or potassium permanganate. Flash column chromatography was carried out using Merck Kieselgel 60 (0.40–0.063 mm diameter) silica.[19] Dry flash chromatography was performed on Merck Kieselgel 60 H and on Sorbsil® silica gel using suction in place of head pressure.[20] Solvents and reagents were dried or purified according to the procedures described by Perrin and Armarego.[21]

3,3′-Disulfanediyldipropanamide **1**.—Thionyl chloride (114.1 g, 70 cm^3, 959 mmol, 4 equiv.) was added to 3,3′-disulfanediyldipropanoic acid (50.0 g, 238 mmol, 1 equiv.) containing pyridine (6 drops) and the mixture was stirred for 48 h at room temperature to give an amber solution. The excess of thionyl chloride was removed at reduced pressure and the crude acid chloride was transferred *via* a cannula into a biphasic system of aqueous ammonia (*d* 0.880, 50 cm^3) and toluene (290 cm^3) at 0 °C; the mixture was then stirred at room temperature overnight. The resulting precipitate was filtered off to give a colourless powder (36.6 g, 74%) m.p. 168–169 °C (lit.,[5] 169–171 °C) after recrystallisation (EtOAc); ν_{max}(KBr)/cm^{-1} 3365 (NH), 3177 (CH), 1652 (CONH) and 1540 (CON); δ_H(200 MHz; CD_3OD) 3.30 (4 H, t, *J* 6.0, CH_2CONH) and 2.90 (4 H, t, *J* 6.0, CH_2S); *m/z* (CI, NH_3) 209 (MH^+, 100%).

Isothiazol-3(2H)-one **2**.—3,3′-Disulfanediyldipropanamide (21.0 g, 100 mmol, 1 equiv.) was suspended in 1,2-dichloroethane (430 cm^3) with stirring at 0 °C and sulfuryl chloride (49.9 g, 26 cm^3, 315 mmol, 3.2 equiv.) was added *via* a cannula. When addition was complete, the flask was allowed to warm to room temperature and the mixture was stirred for 16 h. The precipitate was filtered off and dissolved in warm water (100 cm^3). The undissolved residue was filtered off and the filtrate was diluted with brine (50 cm^3) and continuously extracted with diethyl ether (250 cm^3). The pure product was obtained as colourless needles (1.94 g, 10%), m.p. 74–75 °C (lit.,[5] 73–74 °C) (Found: C, 35.5; H, 2.7; N, 14.0; S, 31.8. Calc. for C_3H_3NSO: C, 35.6; H, 2.99; N, 13.9; S, 31.7%); ν_{max}(KBr)/cm^{-1} 3490 (NH), 1701 (CONH) and 1587 (CONH); δ_H(200 MHz; $CDCl_3$) 10.4 (1 H, s, NH), 8.05 (1 H, d, *J* 5.0, vinyl CH) and 6.60 (1 H, d, *J* 5.0, vinyl CH); *m/z* (CI, NH_3) 209 (MH^+, 100%).

5-Chloroisothiazol-3(2H)-one **3**. Co-product with **2**. Obtained as colourless crystals (0.68 g, 5%), m.p. 95–96 °C (lit.,[5] 95–96 °C) after recrystallisation from water; ν_{max}(KBr)/cm^{-1} 3450 (NH), 1685 (CO), 1550 (CON) and 775 (Cl); δ_H(200 MHz; $CDCl_3$) 6.55 (1 H, s, vinyl CH); *m/z* (CI, NH_3) 137/135 (MH^+, 15%, 100%).

3-(Z)-(*Benzylsulfanyl*)*propenoic Acid* **8**.—To a solution of sodium carbonate (17.5 g, 165 mmol, 1.1 equiv.) in water (200 cm^3), was added propynoic acid (10.6 g, 150 mmol, 1 equiv.), followed by methanol (150 cm^3). Toluene-α-thiol (18.6 g, 17.6 cm^3, 150 mmol, 1 equiv.) was added rapidly to the mixture which was then refluxed for 4 h. After cooling to room temperature the reaction mixture was carefully acidified with 2 mol dm^3 hydrochloric acid (200 cm^3) and extracted with ethyl acetate (3 × 100 cm^3). The combined extracts were washed with water (2 × 100 cm^3) and brine (100 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure to furnish the crude product. The pure product was obtained as colourless needles (24.7 g, 85%), m.p. 138–139 °C (lit,[12] 138–139 °C) after recrystallisation (acetone–hexanes); ν_{max}(KBr)/cm^{-1} 3467 (OH), 1680 (conj. CO) and 1602 (Ph); δ_H(200 MHz; $CDCl_3$) 7.34 (5 H, s, Ph), 7.21 (1 H, d, *J* 10.3, $CHCO_2H$), 5.85 (1 H, s, *J* 10.3, CHS) and 3.99 (2 H, s, CH_2Ph); *m/z* (CI, NH_3) 212 (MNH_4^+, 100%), 195 (MH^+, 40), 108 (40) and 91 (55).

4-*Nitrophenyl* (Z)-3-(*Benzylsulfanyl*)*propenoate* **9**.—To a solution of 4-nitrophenol (3.52 g, 25 mmol, 1.1 equiv.) and (*Z*)-3-(benzylsulfanyl)propenoic acid (4.44 g, 23 mmol, 1 equiv.) in THF (50 cm^3) was added *N,N*-dicyclohexylcarbodiimide (5.16 g, 25 mmol, 1.1 equiv.) in THF (50 cm^3) and the mixture was stirred under nitrogen for 16 h. It was then filtered through a 3 cm pad of silica, eluting with diethyl ether–pentane (1:1) and the solvent was removed under reduced pressure to yield the crude product as a pale yellow solid. The pure product was obtained as colourless needles, m.p. 123–124 °C after recrystallisation (EtOAc–hexanes) (5.58 g, 73%) (Found: C, 61.2; H, 4.2; N, 4.4. $C_{16}H_{13}NO_4S$ requires C, 60.9; H, 4.15; N, 4.4%); ν_{max}(KBr)/cm^{-1} 3073, 2930, 2850 (CH), 1704 (CO_2R), 1674 (C=C), 1592 and 1558 (NO_2) and 1353 ($ArNO_2$); δ_H(200 MHz; $CDCl_3$) 8.26 (2 H, m, AA'BB', Ar), 7.50–7.30 (8 H, m, AA'BB', Ar, Ph and vinylic CH), 6.10 (2 H, d, *J* 10.0, SCH) and 4.04 (2 H, s, SCH_2Ph); *m/z* (CI, NH_3) 333 (MNH_4^+, 70%), 316 (10, MH^+), 177 (100) and 91 (60).

N-[(Z)-3-*Benzylsulfanylpropenoyloxy*]*succinimide* **10**.—To a solution of (*Z*)-3-(benzylsulfanyl)propenoic acid (3.33 g, 17 mmol, 1 equiv.) and *N*-hydroxysuccinimide (2.30 g, 20 mmol, 1.2 equiv.) in THF (120 cm^3) at room temperature was added *N,N*-dicyclohexylcarbodiimide (3.51 g, 17 mmol, 1 equiv.) and the mixture stirred for 24 h under nitrogen. The precipitated dicyclohexylurea was filtered off and the filtrate was diluted with diethyl ether (70 cm^3), washed with brine (2 × 70 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure to give the crude product. This was recrystallised (EtOAc–hexanes) to furnish the pure product as colourless needles, m.p. 160–160.5 °C (2.22 g, 44%); ν_{max}(KBr)/cm^{-1} 2980 (CH), 1751 (conj. CO_2R and imide) and 1561 (Ph); δ_H(200 MHz; $CDCl_3$) 7.47 (1 H, d, *J* 10.3, $CHCO_2R$), 7.38–7.29 (5 H, m, Ph), 7.21 (1 H, s, *J* 10.3, CHCON), 6.03 (1 H, s, *J* 10.3, CHS), 4.05 (2 H, s, CH_2Ph) and 2.85 (4 H, s, CH_2); *m/z* (CI, NH_3) 309 (MNH_4^+, 55%), 194 (70) and 177 (100).

1-[(Z)-3-*Benzylsulfanylpropenoyloxy*]*imidazole* **11**.—Carbonyldiimidazole (1.70 g, 10.5 mmol, 1 equiv.) was added to a solution of (*Z*)-3-(benzylsulfanyl)propenoic acid (2.04 g, 10.5 mmol, 1 equiv.) in THF (20 cm^3) under nitrogen and the mixture stirred for 1 h. The mixture was diluted with ethyl acetate (20 cm^3), washed with water (2 × 20 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure to give the crude product which was obtained as colourless needles, m.p. 107–108 °C after recrystallisation (EtOAc–hexanes) (1.78 g, 80%) (Found: C, 63.7; H, 4.9; N, 11.8. $C_{13}H_{12}N_2OS$ requires C, 63.7; H, 4.95; N, 11.5%); ν_{max}(KBr)/cm^{-1} 2980 (CH), 1672 (conj. CO_2N), 1614 (Ph) and 1550 (CON); δ_H(200 MHz; $CDCl_3$) 8.21 (1 H, s, NCHN), 7.62 (1 H, d, *J* 9.9, $CHCO_2N$), 7.51 (1 H, s, NC*H*CH), 7.33 (5 H, s, Ph), 7.11 (1 H, s, NCH), 6.51 (1 H, s, *J* 9.9, CHS) and 4.08 (2 H, s, CH_2Ph); *m/z* (CI, NH_3) 245 (MH^+, 80%), 177 (40) and 69 (100).

General Method for Formation of the Amides **14a–j** *using Diphenylphosphinic Chloride*.[18]—Diphenylphosphinic chloride (1.1 equiv.) was added to a solution of (*Z*)-3-(benzylsulfanyl)-propenoic acid (1 equiv.) and *N*-methylmorpholine (2.2 equiv.) in THF (2 cm^3 $mmol^{-1}$) under nitrogen at −10 °C and the mixture was stirred for 30 min. The requisite amine (1 equiv.) in THF solution was added dropwise to the resultant suspension (in the case of methylamine and ethylamine excess of the gas was bubbled through). The mixture was allowed to warm to room temperature and stirred until TLC analysis showed consumption of the amine. The reaction was diluted with an equal volume of diethyl ether washed with 2 mol dm^3 aqueous sodium hydroxide, 1 mol dm^3 hydrochloric acid and brine, dried ($MgSO_4$) and concentrated under reduced pressure to give the crude product which was purified by recrystallisation.

(Z)-3-(*Benzylsulfanyl*)-N-*methylpropenamide* **14a**. Colourless needles, m.p. 88–89 °C after recrystallisation (EtOAc–hexanes) (253 mg, 71%) (Found: C, 64.0; H, 6.15; N, 6.6. $C_{11}H_{13}NOS$ requires C, 63.7; H, 6.32; N, 6.8%) ν_{max}($CHCl_3$)/cm^{-1} 3397 (NH), 2950 (CH), 1362 (conj. CON), 1575 (Ph) and 1540 (CONH); δ_H(200 MHz; $CDCl_3$) 7.33 (5 H, m, Ph), 6.79 (1 H, d, *J* 10.0, vinylic CH), 5.72 (1 H, d, *J* 10.0, vinylic CH), 5.43 (1 H, br s, NH), 3.92 (2 H, s, SCH_2Ph) and 2.85 (3 H, d, *J* 4.8, CH_3); *m/z* (CI, NH_3) 208 (MH^+, 100%) and 86 (100).

(Z)-3-(*Benzylsulfanyl*)-N-*ethylpropenamide* **14b**. Colourless needles, m.p. 72–73 °C after recrystallisation (EtOAc–hexanes) (0.91 g, 69%); ν_{max}(KBr)/cm^{-1} 3263 (NH), 3058, 2950 and 2874 (CH), 1627 (CONH), 1571 (Ph) and 1542 (CONH); δ_H(200 MHz; $CDCl_3$) 7.37–7.28 (5 H, m, Ph), 6.73 (1 H, d, *J* 10, vinylic CH), 5.74 (1 H, d, *J* 10, vinylic CH), 3.91 (2 H, s, SCH_2Ph), 3.34 (2 H, q, *J* 7.3, NCH_2) and 1.16 (3 H, t, *J* 7.3, CH_3); *m/z* (CI, NH_3) 222 (MH^+, 100%).

(Z)-3-(*Benzylsulfanyl*)-N-*propylpropenamide* **14c**. Colourless needles, m.p. 108–109 °C after recrystallisation (EtOAc–hexanes) (232 mg, 58%) (Found: C, 66.6; H, 7.5; N, 6.1; S, 13.4. $C_{13}H_{17}NOS$ requires C, 66.3; H, 7.28; N, 6.0; S, 13.6%) ν_{max}(KBr)/cm^{-1} 3314 (NH), 3062, 2927, 2868 (CH), 1628 (CON) and 1538 (CONH); δ_H(200 MHz; $CDCl_3$) 7.37 (5 H, s, Ph), 6.80 (1 H, d, *J* 10.0, vinylic CH), 5.71 (1 H, d, *J* 10.0, vinylic CH), 5.50 (1 H, br s, NH), 3.91 (2 H, s, SCH_2Ph), 3.26 (2 H, dt, *J* 7.2 and 4.4, NCH_2), 1.50 (2 H, tq, *J* 7.2 and 7.7, $CH_3CH_2CH_2N$), 0.95 (3 H, t, *J* 7.7, CH_3); *m/z* (CI, NH_3) 236 (MH^+, 100%), 144 (50) and 91 (30).

(Z)-3-(*Benzylsulfanyl*)-N-*isopropylpropenamide* **14d**. Colourless needles, m.p. 120–121 °C after recrystallisation (EtOAc–hexanes) (437 mg, 82%); ν_{max}($CHCl_3$)/cm^{-1} 3437 (NH), 2950 (CH), 1637 (CONH), 1560 (Ph) and 1547 (CONH); δ_H(200 MHz; $CDCl_3$) 7.29 (5 H, m, Ph), 6.78 (1 H, d, *J* 10.0, vinylic CH), 5.67 (1 H, d, *J* 10.0, vinylic CH), 5.25 (1 H, br s, NH), 4.60–4.11 (1 H, m, Me_2CH), 3.91 (2 H, s, SCH_2Ph), 1.16 [6 H, d, *J* 6.8, $CH_3)_2CH$]; *m/z* (CI, NH_3) 236 (100%, MH^+).

(Z)-3-(*Benzylsulfanyl*)-N-tert-*butylpropenamide* **14e**. Colourless needles, m.p. 99–100 °C after recrystallisation (EtOAc–hexanes) (356 mg, 85%); ν_{max}($CHCl_3$)/cm^{-1} 3437 (NH) 2960 (CH), 1651 (CONH) and 1547 (CONH); δ_H(200 MHz; $CDCl_3$) 7.33 (5 H, m, Ph), 6.76 (1 H, d, *J* 10.0, vinylic CH), 5.64 (1 H, d, *J* 10.0, vinylic CH), 3.91 (2 H, s, SCH_2Ph) and 1.37 [9 H, s, *J* 6.8 $(CH_3)_3N$]; *m/z* (CI, NH_3) 250 (MH^+, 100%).

(Z)-3-(*Benzylsulfanyl*)-N-(5-*cyanopentyl*)*propenamide* **14f**. Colourless needles, m.p. 68–69 °C after recrystallisation (EtOAc–hexanes) (814 mg, 62%) (Found: C, 66.6; H, 7.12; N, 9.6. $C_{16}H_{20}NOS$ requires C, 66.6; H, 6.99; N, 9.7%) ν_{max}(KBr)/cm^{-1} 3372 (NH), 3083, 3060, 3023 (CH), 2864 (CN),

1650 (CONH), 1569 (C=C) and 1517 (CONH); δ_H(200 MHz; $CDCl_3$) 7.34 (5 H, m, Ph), 6.81 (1 H, d, *J* 10.0, vinylic CH), 5.71 (1 H, d, *J* 10.0, vinylic CH), 5.55 (1 H, br s, NH), 3.91 (2 H, s, SCH_2Ph), 3.30 (2 H, dt, *J* 6.4 and 6.2, $NHCH_2$), 2.34 (2 H, t, *J* 6.7, CH_2CN) and 1.90–1.30 (6 H, m, CH_2); *m/z* (CI, NH_3) 289 (MH^+, 100%), 197 (50) and 91 (40).

(Z)-3-(*Benzylsulfanyl*)-N-*phenylpropenamide* **14g**. Colourless leaflets, m.p. 167–169 °C after recrystallisation (EtOAc–hexanes) (1.67 g, 62%) (Found: C, 71.6; H, 5.7; N, 5.2. $C_{16}H_{20}NOS$ requires C, 71.3; H, 5.61; N, 5.2%) ν_{max}(KBr)/cm^{-1} 3227 (NH), 3031, 2910, 2691 (CH), 1637 (CONH), 1594 (Ph and C=C) and 1567 (CONH); δ_H(200 MHz; $CDCl_3$) 7.58 (2 H, m, Ar–N), 7.36–7.30 (5 H, m, Ph), 7.26–7.12 (4 H, m, Ar–N and NH), 7.02 (1 H, d, *J* 9.9, vinylic CH), 5.93 (1 H, d, *J* 9.9, vinylic CH) and 3.96 (2 H, s, SCH_2Ph); *m/z* (CI, NH_3) 270 (MH^+, 100%).

(Z)-3-(*Benzylsulfanyl*)-N-(4-*methoxyphenyl*)*propenamide* **14h**. Colourless needles, m.p. 111–112 °C after recrystallisation (EtOAc–hexanes) (2.50 g, 83%); ν_{max}(KBr)/cm^{-1} 3285 (NH), 2970, 2929 and 2831 (CH), 1657 (CONH), 1636 (Ph), 1606 (C=C), 1581 (Ar) and 1517 (CONH); δ_H(200 MHz; $CDCl_3$) 7.50–7.29 (7 H, m, Ar), 7.07 (1 H, br s, NH), 6.93 (1 H, d, *J* 9.9, vinylic CH), 6.84 (2 H, m, ArH), 5.85 (1 H, d, *J* 9.9, vinylic CH), 3.95 (2 H, s, SCH_2Ph) and 3.79 (3 H, s, OCH_3); *m/z* (CI, NH_3) 300 (MH^+, 100%).

(Z)-3-(*Benzylsulfanyl*)-N-[(4-*ethoxycarbonyl*)*phenyl*]*propenamide* **14i**. Oxalyl chloride (1.57 g, 1.1 cm^3, 12.4 mmol, 1.2 equiv.) was added to a solution of (*Z*)-3-(benzylsulfanyl)-propenoic acid (2.00 g, 10.3 mmol, 1 equiv.) in dichloromethane (30 cm^3) at room temperature followed by dimethylformamide (3 drops) and the resultant mixture stirred until no further effervescence could be noted. The homogeneous solution was added dropwise to a solution of ethyl 4-aminobenzoate (2.05 g, 12.4 mmol, 1.2 equiv.) and pyridine (1.23 g, 1.3 cm^3, 15.5 mmol, 1.5 equiv.) in dichloromethane (50 cm^3) at −20 °C. The reaction mixture was stirred for 6 h, after which it was washed with 1 mol dm^{-3} hydrochloric acid (3 × 50 cm^3), saturated aqueous sodium hydrogen carbonate (50 cm^3) and brine (50 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure to give the crude product. The pure product was obtained as colourless needles, m.p. 126–127 °C after recrystallisation (EtOAc–hexanes) (2.43 g, 69%) (Found: C, 67.1; H, 5.5; N, 4.1. $C_{19}H_{19}NO_3S$ requires C, 66.8; H, 5.61; N, 4.1%) ν_{max}(KBr)/cm^{-1} 3366 (NH), 3049, 2984, 2905 (CH), 1734 (conj. CO_2R), 1697 (CONH), 1610 (C=C), 1543 (CONH) and 1471 (C–O); δ_H(200 MHz; $CDCl_3$) 7.97 (2 H, AA'BB', ArH), 7.65 (2 H, AA'BB', ArH), 7.53 (1 H, br s, NH), 7.32 (5 H, s, Ph), 7.05 (1 H, d, *J* 9.9, vinylic CH), 5.92 (2 H, d, *J* 9.9, vinylic SCH), 4.35 (2 H, q, *J* 7.1, CH_2CH_3), 4.04 (2 H, s, SCH_2Ph) and 1.38 (3 H, t, *J* 7.1, CH_2CH_3); *m/z* (CI, NH_3) 342 (MH^+, 10%), 283 (100), 266 (95).

(Z)-3-(*Benzylsulfanyl*)-N-(4-*nitrophenyl*)*propenamide* **14j**. Oxalyl chloride (1.60 g, 1.1 cm^3, 12.6 mmol, 1.2 equiv.) was added to a solution of (*Z*)-3-(benzylsulfanyl)propenoic acid (2.04 g, 10.5 mmol, 1 equiv.) in dichloromethane (30 cm^3) at room temperature followed by dimethylformamide (3 drops) and the resultant mixture stirred until no further effervescence could be noted. The homogeneous solution was added dropwise to a solution of *p*-nitroaniline (3.19 g, 23.1 mmol, 2.2 equiv.) in THF (50 cm^3) at below −20 °C. The reaction mixture was stirred for 6 h after which it was washed with 1 mol dm^{-3} hydrochloric acid (3 × 50 cm^3), saturated aqueous sodium hydrogen carbonate (50 cm^3) and brine (50 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure to give the crude product, obtained as colourless needles, m.p. 153–154 °C after recrystallisation (EtOAc–hexanes) (1.06 g, 62%) (Found: C, 60.8; H, 4.4; N, 8.6. $C_{16}H_{14}N_2O_3S$ requires C, 61.1; H, 4.49; N, 8.9%) ν_{max}(KBr)/cm^{-1} 3394 (NH), 3033 (ArH), 2926 (CH), 1666 (CONH), 1606 (C=C), 1595 (Ph), 1535 (CONH), 1505 and 1325 (NO_2); δ_H(200 MHz; $CDCl_3$) 8.18 (2 H, AA'BB', ArH), 7.78 (2 H, AA'BB', ArH), 7.43 (1 H, br s, NH), 7.37–7.28 (5 H, m, Ph), 7.14 (1 H, d, *J* 9.9, vinylic CH), 5.90 (1 H, d, *J* 9.9, vinylic CH) and 4.01 (2 H, s, SCH_2Ph); *m/z* (CI, NH_3) 315 (MH^+, 100%).

General Method for Formation of Sulfoxides **15a–j**.—To a solution of the sulfide in dichloromethane (5 cm^3 $mmol^{-1}$), was added dropwise a solution of 3-chloroperbenzoic acid (1 equiv.) in dichloromethane (5 cm^3 $mmol^{-1}$), the temperature being kept < 0 °C; the mixture was then stirred for 10 min at −10 to −5 °C. The reaction was quenched by the addition of aqueous sodium hydrogen sulfite (10 cm^3), washed with saturated aqueous sodium hydrogen carbonate (2 × 10 cm^3) and brine (20 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. The crude products were purified either by recrystallisation or flash chromatography on silica eluting with ethyl acetate–hexanes.

(Z)-3-(*Benzylsulfinyl*)-N-*methylpropenamide* **15a**. Colourless needles, m.p. 114–115 °C after recrystallisation (EtOAc–hexanes) (386 mg, 69%) (Found: C, 59.4; H, 5.6; N, 6.5. $C_{11}H_{13}NO_2S$ requires C, 59.2; H, 5.87; N, 6.3%) ν_{max}(KBr)/cm^{-1} 3275 (NH), 3063, 2958, 2934 (CH), 1658 (CONH), 1627 (C=C), 1598 (Ph), 1545 (CONH) and 1025 (SO); δ_H(200 MHz; $CDCl_3$) 7.41 (5 H, m, Ph), 6.61 (1 H, br s, NH), 6.37 (1 H, d, *J* 10.1, vinylic CH), 6.27 (1 H, d, *J* 10.1, vinylic CH), 4.37 (1 H, d, *J* 12.6, SCH_2Ph), 4.18 (1 H, d, *J* 12.6, SCH_2Ph) and 2.85 (3 H, d, *J* 4.9, CH_3); *m/z* (CI, NH_3) 224 (MH^+, 100%) and 116 (40).

(Z)-3-(*Benzylsulfinyl*)-N-*ethylpropenamide* **15b**. Colourless needles, m.p. 120–121 °C after recrystallisation (EtOAc–hexanes) (860 mg, 89%) (Found: C, 61.0; H, 6.2; N, 5.7. $C_{12}H_{15}NO_2S$ requires C, 60.7; H, 6.37; N, 5.9%) ν_{max}(KBr)/cm^{-1} 3255 (NH), 3068, 2972 and 2931 (CH), 1659 (CONH), 1605 (C=C), 1556 (CONH) and 1069 (SO); δ_H(200 MHz; $CDCl_3$) 7.39 (5 H, m, Ph), 6.37 (2 H, d + br s, *J* 10.1, superimposed vinylic CH and NH), 6.18 (1 H, d, *J* 10.1, vinylic CH), 4.36 (1 H, d, *J* 12.6, PhC*H*S), 4.12 (1 H, d, *J* 12.6, PhCH_2S), 3.35 (2 H, q, *J* 7.3, OCH_2) and 1.18 (1 H, t, *J* 7.3, CH_3); *m/z* (CI, NH_3) 238 (MH^+, 100%) and 130 (40).

(Z)-3-(*Benzylsulfinyl*)-N-*propylpropenamide* **15c**. Colourless needles, m.p. 103–104 °C after recrystallisation (EtOAc–hexanes) (206 mg, 87%) (Found: C, 62.4; H, 6.8; N, 5.6; S, 12.8. $C_{13}H_{17}NOS$ requires C, 62.4; H, 6.81; N, 5.4; S, 12.6%) ν_{max}(KBr)/cm^{-1} 3876 (NH), 2927 and 2868 (CH), 1747 (CONH), 1654 (C=C), 1603 (Ph), 1538 (CONH) and 1068 (SO); δ_H(200 MHz; $CDCl_3$) 7.37 (5 H, m, Ph), 6.40 (1 H, d, *J* 10.0, vinylic CH), 6.22 (1 H, d, *J* 10.0, vinylic OSCH), 4.35 (1 H, d, *J* 12.6, OSC*H*Ph), 4.25 (1 H, d, *J* 12.6, OSC*H*Ph), 3.30 (2 H, dt, *J* 7.2 and 6.7, NCH_2), 1.60 (2 H, tq, *J* 7.2 and 7.7, $CH_3CH_2CH_2N$) and 0.96 (3 H, t, *J* 7.7, CH_3); *m/z* (CI, NH_3) 252 (MH^+, 100%) and 141 (50).

(Z)-3-(*Benzylsulfinyl*)-N-*isopropylpropenamide* **15d**. The title product was obtained as clear colourless needles, m.p. 124 °C after recrystallisation (EtOAc–hexanes) (514 mg, 90%) (Found: C, 62.0; H, 6.9; N, 5.8. $C_{13}H_{17}NO_2S$ requires C, 62.1; H, 6.82, N, 5.6%); ν_{max}(KBr)/cm^{-1} 3253 (NH), 2970, 2929, 2789 (CH), 1658 (CONH), 1600 (C=C, Ph), 1551 (CONH) and 1023 (SO); δ_H(200 MHz; $CDCl_3$) 7.40–7.33 (5 H, m, Ph), 6.43 (1 H, d, *J* 10.1, vinylic CH), 6.22 (1 H, d, *J* 10.1, vinylic CH), 6.02 (1 H, br s, NH), 4.36 (1 H, d, *J* 12.6, SCH_2Ph), 4.22 (1 H, d, *J* 12.6, SCH_2Ph), 4.11 (1 H, m, C*H*Me_2), 1.22 [3 H, d, *J* 6.8, $(CH_3)_2CH$] 1.24 [3 H, d, *J* 6.8, $(CH_3)_2CH$]; *m/z* (CI, NH_3) 252 (MH^+, 100%) and 144 (40).

(Z)-3-(*Benzylsulfinyl*)-N-tert-*butyl-propenamide* **15e**. Colourless needles, m.p. 122–123 °C after recrystallisation (EtOAc–hexanes) (225 mg, 74%) (Found: C, 63.3; H, 7.4; N, 5.0. $C_{14}H_{19}NO_2S$ requires C, 63.4; H, 7.22; N, 5.3%) ν_{max}(KBr)/

cm^{-1} 3280 (NH), 3066, 2973 and 2770 (CH), 1658 (CONH) 1603 (C=C, Ph), 1551 (CONH) and 1016 (SO); δ_H(200 MHz; $CDCl_3$) 7.40 (5 H, s, Ph), 6.31 (1 H, d, *J* 10.0, vinylic CH), 6.23 (1 H, d, *J* 10.0, vinylic CH), 5.98 (1 H, br s, NH), 4.63 (1 H, d, *J* 12.0, SCH_2Ph), 4.33 (1 H, d, *J* 12.0, SCH_2Ph) and 1.40 [9 H, s, $(CH_3)_3N$]; *m/z* (CI, NH_3) 266 (MH^+, 100%).

(Z)-3-(*Benzylsulfinyl*)-N-(5-*cyanopentyl*)*propenamide* **15f**. Colourless oil after flash chromatography on silica, eluting with ethyl acetate (804 mg, 87%) (Found: C, 63.9; H, 5.4; N, 3.9. $C_{16}H_{20}NO_2S$ requires C, 63.7; H, 5.01; N, 3.8%) ν_{max}(KBr)/ cm^{-1} 3262 (NH), 3064, 2936 and 2866 (CH), 2245 (CN), 1661 (CONH), 1606 (C=C), 1536 (CONH) and 1023 (SO); δ_H(200 MHz; $CDCl_3$) 7.37 (5 H, s, Ph), 6.60 (1 H, d, *J* 10.1, vinylic CH), 6.23 (1 H, d, *J* 10.1, vinylic CH), 4.35 (1 H, d, *J* 12.6, OSC*H*Ph), 4.17 (1 H, d, *J* 12.6, OSC*H*Ph), 3.33 (2 H, dt, *J* 6.5 and 6.3, $NHCH_2$), 2.38 (2 H, t, *J* 6.8, CH_2CN) and 1.74–1.53 (6 H, m, CH_2); *m/z* (CI, NH_3) 305 (MH^+, 95%), 197 (50), 108 (20), 91 (95).

(Z)-3-(*Benzylsulfinyl*)-N-*phenylpropenamide* **15g**. The title compound was obtained as colourless leaflets, m.p. 178–179 °C after recrystallisation (EtOAc–hexanes) (1.66 g, 90%); ν_{max}-(KBr)/ cm^{-1} 3227 (NH), 3031, 2910, 2691 (CH), 1637 (CONH), 1594 (Ph and C=C) and 1567 (CONH); δ_H(200 MHz; $CDCl_3$) 7.58 (2 H, m, N–ArH), 7.36–7.30 (5 H, m, Ph), 7.26–7.12 (4 H, m, N–ArH and NH), 7.02 (1 H, d, *J* 9.9, vinylic CH), 5.93 (1 H, d, *J* 9.9, vinylic CH) and 3.96 (2 H, s, SCH_2Ph); *m/z* (CI, NH_3) 286 (MH^+, 75%), 178 (100).

(Z)-3-(*Benzylsulfinyl*)-N-(4-*methoxyphenyl*)*propenamide* **15h**. Colourless needles, m.p. 173–174 °C after recrystallisation (EtOAc–hexanes) (891 mg, 69%) (Found: C, 64.6; H, 5.3; N, 4.4. $C_{17}H_{17}NO_3S$ requires C, 64.7; H, 5.43; N, 4.4%) ν_{max}(KBr)/ cm^{-1} 3248 (NH), 2957, 2928, 2830 (CH), 1667 (CONH), 1622 (Ph), 1604 (C=C), 1558 (CONH) and 1014 (SO); δ_H(200 MHz; $CDCl_3$) 8.60 (1 H, br s, NH), 7.48 (2 H, AA'BB', Ar), 7.39–7.32 (5 H, m, Ph), 6.85 (2 H, AA'BB', Ar), 6.39 (2 H, br s, vinylic CH), 4.41 (1 H, d, *J* 12.7, SC*H*Ph), 4.24 (1 H, d, *J* 12.7, SC*H*Ph) and 3.81 (3 H, s, OCH_3); *m/z* (CI, NH_3) 315 (MH^+, 100%) and 208 (60).

(Z)-3-(*Benzylsulfinyl*)-N-[4-(*ethoxycarbonyl*)*phenyl*]*propenamide* **15i**. Colourless needles, m.p. 170–171 °C after recrystallisation ($CHCl_3$–hexanes) (2.02 g, 91%); ν_{max}(KBr)/ cm^{-1} 3366 (NH), 3049, 2984, 2905 (CH), 1703 (CO_2R), 1673 (CONH), 1600 (C=C), 1546 (CONH), 1471 (C–O) and 1026; δ_H(500 MHz; $CDCl_3$) 9.24 (1 H, s, NH), 8.02 (2 H, AA'BB', Ar), 7.66 (2 H, AA'BB', Ar), 7.32 (5 H, m, Ph), 6.49 (1 H, d, *J* 10.5, vinylic CH), 6.46 (1 H, d, *J* 10.5, vinylic SCH), 4.44 (1 H, d, *J* 12.8, SCH_2Ph, 4.38 (2 H, q, *J* 7.1, CH_2CH_3), 4.26 (2 H, d, *J* 12.8, SCH_2Ph) and 1.41 (3 H, t, *J* 7.1, CH_2CH_3); *m/z* (CI, NH_3) 358 (MH^+, 20%), 250 (100) and 108 (40).

(Z)-3-(*Benzylsulfinyl*)-N-(4-*nitrophenyl*)*propenamide* **15j**. Colourless needles, m.p. > 250 °C after recrystallisation (DMSO–H_2O) (124 mg, 96%); ν_{max}(KBr)/cm ^{1} 3366 (NH), 3084 (ArH), 2788 (CH), 1685 (CONH), 1625 (C=C), 1596 (Ar), 1567 (CONH), 1506 (NO_2), 1335 (NO_2) and 1029 (SO); δ_H(200 MHz; [$^2H_6$]-DMSO) 10.99 (1 H, br s, NH), 8.25 (2 H, AA'BB', Ar), 8.21 (1 H, d, *J* 10.2, vinylic CH), 7.97 (2 H, AA'BB', Ar), 7.37–7.31 (5 H, s, Ph), 6.65 (1 H, d, *J* 10.2, vinylic SCH), 4.48 (1 H, d, *J* 12.7, SCH_2Ph) and 4.20 (2 H, d, *J* 12.7, SCH_2Ph); *m/z* (CI, NH_3) 331 (MH^+, 100%) and 223 (50).

General Preparation of Isothiazolones **4a–i**.[11]—To a solution of the requisite (Z)-3-(benzylsulfanyl)-*N*-alkylpropenamide **14a–i** in dichloromethane (5 cm^3 $mmol^{-1}$) under an atmosphere of nitrogen at 0 °C, was added trichloroacetic anhydride (1.2 equiv.). The reaction mixture was stirred at 0 °C for 1 h, then warmed to room temperature and stirred for a further 2 h. The reaction was quenched with 2 mol dm^{-3} aqueous sodium hydroxide and the reaction mixture was extracted with dichloromethane. The extract was dried (Na_2SO_4) and concentrated under reduced pressure and the residue purified by chromatography on silica, eluting with ethyl acetate–pentane. Further purification was carried out by sublimation at reduced pressure when required.

N-*Methylisothiazol*-3(2H)-*one* **4a**. Colourless needles (399 mg, 66%), m.p. 51–52 °C after sublimation (100 °C at 1 mmHg) (lit.[8] 50–51 °C); ν_{max}(KBr)/cm^{-1} 3080 (CH), 2969 (CH), 1620 (CONR) and 1450 (CONR); δ_H(200 MHz; $CDCl_3$) 8.02 (1 H, d, *J* 6.2, vinylic CH), 6.27 (1 H, d, *J* 6.2, vinylic CH) and 3.36 (3 H, s, NCH_3); *m/z* (CI, NH_3) 116 (MH^+, 100%).

N-*Ethylisothiazol*-3(2H)-*one* **4b**. Colourless needles (230 mg, 68%), m.p. 61–62 °C (lit.,[8] m.p. 59–61 °C) after sublimation (100 °C at 0.05 mmHg); ν_{max}(KBr)/cm^{-1} 3085 (CH), 2979 (CH), 1626 (CONR) and 1451 (CONR); δ_H(200 MHz; $CDCl_3$) 8.03 (1 H, d, *J* 6.2, vinylic CH), 6.24 (1 H, d, *J* 6.2, vinylic CH), 3.85 (2 H, q, *J* 7.2, NCH_2) and 1.34 (3 H, t, *J* 7.2, CH_2CH_3); *m/z* (CI, NH_3) 130 (MH^+, 100%).

N-*Propylisothiazol*-3(2H)-*one* **4c**.[5] Colourless oil (41 mg, 62%); ν_{max}(film)/cm^{-1} 2966 (CH), 2934 (CH), 1616 (conj. CONH) and 1451 (CONH); δ_H(200 MHz; $CDCl_3$) 8.05 (1 H, d, *J* 6.2, vinylic CH), 6.23 (1 H, d, *J* 6.2, vinylic CH), 3.7 (2 H, t, *J* 7.7, NCH_2), 1.50 (2 H, dt, *J* 7.2 and 7.7, $CH_3CH_2CH_2N$) and 0.95 (3 H, t, *J* 7.2, CH_3); *m/z* (CI, NH_3) 144 (MH^+, 100%).

N-*Isopropylisothiazol*-3(2H)-*one* **4d**. Colourless oil (55 mg, 67%); ν_{max}(KBr)/cm^{-1} 3085 (CH), 2979 (CH), 1626 (CONR) and 1451 (CONR); δ_H(200 MHz; $CDCl_3$) 8.05 (1 H, d, *J* 6.2, vinylic CH), 6.23 (1 H, d, *J* 6.2, vinylic CH), 4.83 [1 H, sept, *J* 6.7, $NCH(CH_3)_2$] and 1.24 [6 H, d, *J* 6.7, $(CH_3)_2CH$]; *m/z* (CI, NH_3) 144 (MH^+, 100%).

N-tert-*Butylisothiazol*-3(2H)-*one* **4e**. Colourless needles (50 mg, 41%), m.p. 83.5 °C (toluene–hexanes; lit.,[5] 85–86 °C); ν_{max}(KBr) 2974 (CH), 2929 (CH), 1742 (CONR) and 1602; δ_H(200 MHz; $CDCl_3$) 7.91 (1 H, d, *J* 6.2, vinylic CH), 618 (1 H, d, *J* 6.2, vinylic CH) and 1.65 [9 H, s, $C(CH_3)_3$]; *m/z* (CI, NH_3) 158 (MH^+, 100%) and 102 (80).

N-(5-*Cyanopentyl*)*isothiazol*-3(2H)-*one* **4f**. Colourless oil (320 mg, 48%); ν_{max}(film) 2950 (CH), 2244 (CN), 1631 (CONR) and 1509; δ_H(200 MHz; $CDCl_3$) 8.10 (1 H, d, *J* 6.2, vinylic CH), 6.25 (1 H, d, *J* 6.2, vinylic CH), 3.83 (2 H, t, *J* 7.6, CH_2CON), 2.40 (2 H, t, *J* 7.6, CH_2CN) and 1.6 (6 H, m, CH_2); *m/z* (CI, NH_3) 214 (MNH_4^+, 10%) and 197 (MH^+, 100%).

N-*Phenylisothiazol*-3(2H)-*one* **4g**. Colourless needles, m.p. 92–93 °C (toluene; lit.,[5] 91–92 °C) (122 mg, 74%); ν_{max}(KBr)/ cm^{-1} 3118 and 2954 (CH), 1628 (CONR) and 1508 (Ar); δ_H(200 MHz; $CDCl_3$) 8.14 (1 H, d, *J* 6.3, vinyl CH), 7.62–2.29 (5 H, m, Ph), 6.34 (1 H, d, *J* 6.3, vinyl CH) and 3.48 (3 H, s, OCH_3); *m/z* (CI, NH_3) 178 (MH^+, 100%).

N-(4-*Methoxyphenyl*)*isothiazol*-3(2H)-*one* **4h**. Colourless needles (674 mg, 65%) m.p. 92–93 °C (toluene; lit.,[5] 91–92 °C); ν_{max}(KBr)/cm^{-1} 3133 (CH), 1625 (CONR) and 1590 (Ar); δ_H(200 MHz; $CDCl_3$) 8.16 (1 H, d, *J* 6.3, vinyl CH), 7.48 (2 H, AA'BB', ArH), 6.96 (2 H, AA'BB', ArH), 6.34 (1 H, d, *J* 6.3, vinyl CH) and 3.84 (3 H, s, OMe); *m/z* (CI, NH_3) 178 (MH^+, 100%).

N-[(4-*Ethoxycarbonyl*)*phenyl*]*isothiazol*-3(2H)-*one* **4i**. Colourless needles (502 mg, 42%) m.p. 143–144 °C (toluene–hexanes; lit.,[5] 141–142 °C); ν_{max}(KBr)/cm^{-1} 3075 (ArH), 2980 (CH), 1715 (conj. CO_2R), 1646 (CONR) and 1603 (C=C); δ_H(200 MHz; $CDCl_3$) 8.19 (1 H, d, *J* 6.4, vinylic CH), 8.12 (2 H, AA'BB', ArH), 7.75 (2 H, AA'BB', ArH), 6.35 (1 H, d, *J* 6.4, vinylic CH), 4.39 (2 H, q, *J* 7.1, OCH_2CH_3) and 1.41 (3 H, t, *J* 7.1, CH_3); *m/z* (CI, NH_3) 250 (MH^+, 100%).

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