The chemistry of 5-oxodihydroisoxazoles. Part 19.[1] The synthesis and photolysis of *N*-thioacylisoxazol-5(2*H*)-ones

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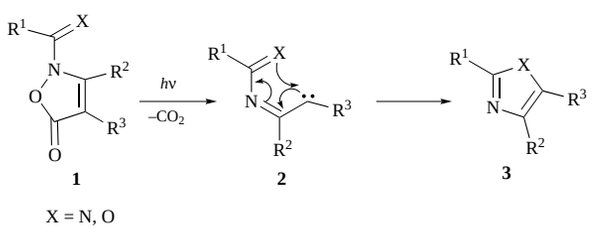
5-Oxodihydroisoxazoles react with thiocarbonyl chlorides to afford *N*-thioacylisoxazol-5(2*H*)-ones which lose carbon dioxide under photochemical conditions and undergo intramolecular cyclisation of the iminocarbene to afford thiazoles. However, in some cases loss of carbon dioxide is accompanied by loss of sulfur, giving 1,3-oxazin-6-ones.

Introduction

We have recently detailed our investigation into the synthesis,[3] and reactions[1] of *N*-acylisoxazol-5(2*H*)-ones **1**, (X = O) which supported previous work[4,5] showing that these molecules form intermediate iminocarbenes **2** which readily react with intramolecular nucleophiles such as nitrogen and oxygen giving imidazoles and oxazoles **3** (X = N or O). A logical extension of this synthesis was to investigate the reactivity of these carbenes in the presence of a C=S bond, in the expectation of achieving a thiazole synthesis (Scheme 1, X = S). Such an outcome



Scheme 1

would be worthwhile because of the increasing discovery of the thiazole ring system in natural products,[6] which has encouraged a number of new syntheses.[7]

The acylation of 5-oxodihydroisoxazoles has previously been complicated by competing 'O' and 'N' acylation, where the product ratio was dictated by both the method chosen, and the nature of the substitution pattern at C3 and C4. However, the number of literature methods for achieving amine thioacylation is far less than for acylation, and usually entails reaction with thiocarbonyl chlorides,[8] dithioesters[9] and amides,[10] dithiocarboxylate salts,[11] thioanhydrides[12] and isothiocyanates.[13] Although treatment of amides with Lawesson's reagent[14] generates thioamides, it was quickly shown that this procedure was incompatible with the presence of ester and lactone groups which are present in the isoxazolone ring system, despite a recent report[15] which shows that modification of this procedure allows selective amine thioacetylation.

We herein report our results on the synthesis of some *N*-thioacylisoxazol-5(2*H*)-ones and their photochemical rearrangements.

Results and discussion

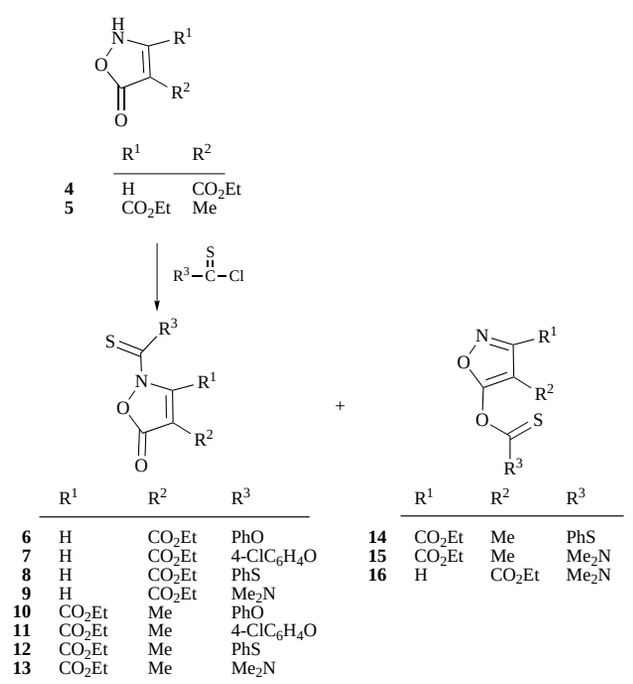
Synthesis

The two 5-oxo-2,5-dihydroisoxazoles used herein were chosen for their propensity to generate the iminocarbene under photochemical conditions when substituted on nitrogen, and because thiazole carboxylic acids were required for other work. Isoxazolone **4** has previously been shown[3] to be readily acylated on nitrogen with acid chlorides, avoiding unwanted *O*-acylated material. When **4** was reacted with a variety of commercially available thiocarbonyl chlorides in the presence of pyridine (Scheme 2), near quantitative yields of *N*-thioacylated products were obtained in most cases (Table 1). Some problems were encountered with thiobenzoyl chloride, dimethylthiocarbamoyl chloride and phenyl isothiocyanate. Phenyl iso-

Table 1 Thioacylation of isoxazol-5-ones

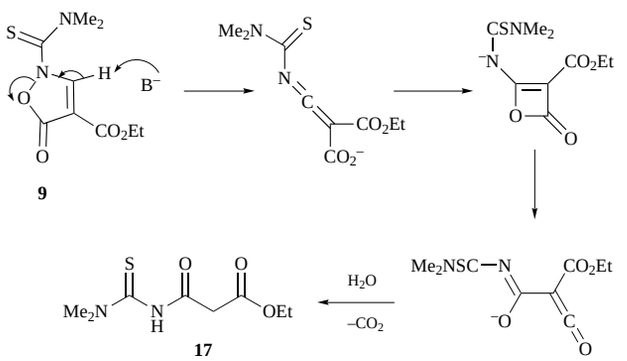
Isoxazolone	Thiocarbonyl chloride RC(S)Cl	*O*-Acylation (%)	*N*-Acylation (%)
4	PhO	0	**6**, 100
	p-ClC_6H_4O	0	**7**, 100
	PhS	0	**8**, 85
	NMe_2	6	**9**, 36
5	PhO	0	**10**, 100
	p-ClC_6H_4O	0	**11**, 98
	PhS	**14**, 57	**12**, 43
	NMe_2	**23**, 19	**13**, 69
	Me[a]	Trace	Trace

[a] Phenylmercury dithioacetate used instead of thioacetyl chloride.



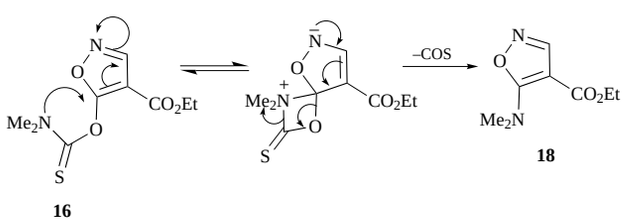
Scheme 2

thiocyanate, surprisingly, failed to react under a variety of conditions with **4** even in the absence of solvent. Reaction of dimethylthiocarbamoyl chloride with **4** at 80 °C in the presence of pyridine gave the imide **17**, by base induced rearrangement[16] of the initial product **9** (Scheme 3), while reaction at 20 °C



Scheme 3

afforded only 46% total acylated product, of which 50% of this was the *O*-acylated compound **16**. However, when this mixture was kept in deuteriochloroform for a number of days, *O*-acyl to *N*-acyl isomerisation was observed, affording 86% *N*-acylated material **9** together with **16** and a trace of a new compound, **18**. When the 1:1 mixture of **9** and **16** was heated in benzene to hasten this isomerisation, the only products obtained were **18** and the 1,3-oxazin-6-one **20**. These products are formed independently of each other: isoxazole **18** could be derived from an intramolecular rearrangement of the *O*-acylated material **16**, involving ipso substitution aided by the ethoxycarbonyl group (Scheme 4). The 1,3-oxazin-6-one **20** could be



Scheme 4

derived from the ring opened ketene **19** which eliminates sulfur. Two pathways may be envisaged for this loss of sulfur, one of which is somewhat similar to the rearrangement of aromatic *N*-oxides reported by Streith and Martz[17] (Scheme 5). The reaction of **4** with thiobenzoyl chloride also followed this pathway giving the 1,3-oxazin-6-one **21**. 1,3-Oxazin-6-ones have previously been reported from the reactions of isoxazolones, but by totally different pathways.[18–22]

The isoxazolone **5**,[23] substituted at C3, did not undergo the base induced rearrangements observed above. When **5** was reacted with thiocarbonyl chlorides in the presence of pyridine, near quantitative yields of the *N*-acylated products **10** and **11** were obtained (Table 1). Reaction of **5** with phenylsulfanylthiocarbonyl chloride at room temperature gave 43% of the *N*-acylated material **12**, and 57% *O*-acylated material **14**. When the temperature was raised to 80 °C, these reactants gave **22** (84%), analogous to the reaction of **4** with dimethylthiocarbamoyl chloride leading to **20**, noted above. Acylation with dimethylcarbamoyl chloride gave only 69% *N*-acylated material **13**, together with some *O*-acylated **15**. No rearrangement akin to that leading to the formation of **18** was observed, as expected from the inability of the ethoxycarbonyl group to stabilise the required intermediate. The use of thiophosgene under various conditions gave only diacylated material and was not further investigated, and again no reaction was observed with phenyl isothiocyanate.

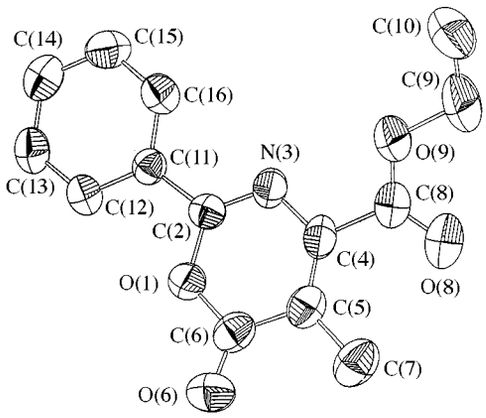


Fig. 1 Molecular structure of **23**, shown with displacement ellipsoids drawn at the 50% probability level

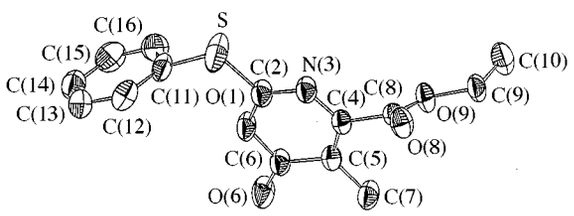
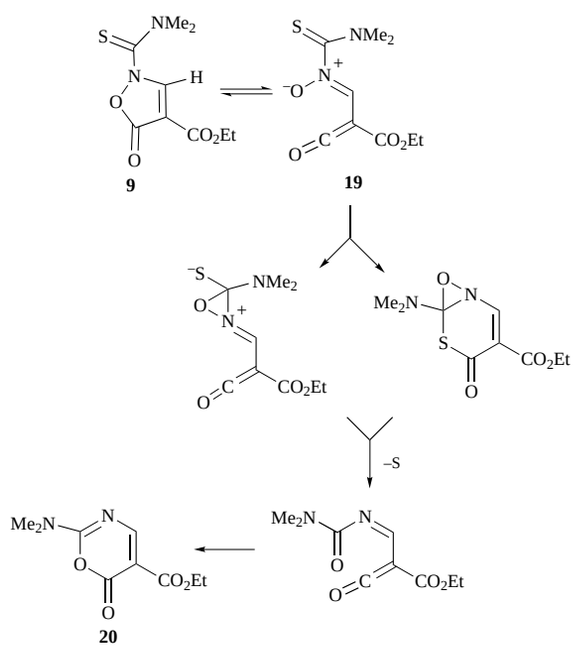


Fig. 2 Molecular structure of **22**, shown with displacement ellipsoids drawn at the 50% probability level



Scheme 5

Attempts to thioacetylate **5** using reagents other than thiocarbonyl chlorides, *e.g.* dithioesters,[9] dithiocarboxylates[11] and carbodiimide coupling agents were unsuccessful. Only trace amounts were obtained with the use of phenylmercury dithioacetate.[11d]

The structures of the 1,3-oxazin-6-ones **23** and **22**, where **23** was derived from the reaction of thiobenzoyl chloride with **5** at room temperature, were confirmed by single crystal X-ray analysis (Figs. 1 and 2).

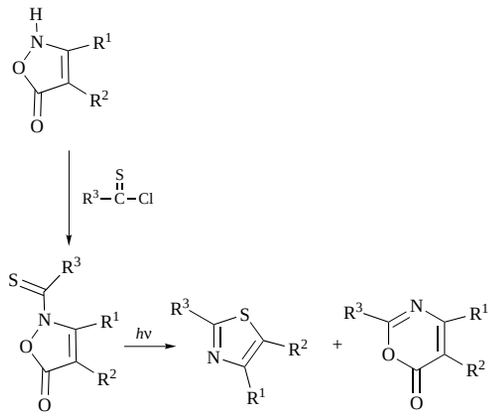
Photolysis

Optimum photolyses of *N*-thioacylisoxazolones were conducted in acetone at 300 nm and were found to be complete within 30 min; the results are compiled in Table 2. The photochemical reactions observed are summarised in Scheme 6.

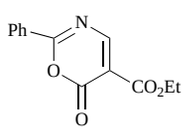
The photolysis of the three *N*-thioacylisoxazolones **6**–**8**

Table 2 Products from photolysis of *N*-thioacylisoxazol-5-(2*H*)-ones at 300 nm

Isoxazolone	R	Oxazine (%)	Thiazole (%)
6	PhO		**27**, 65
7	4-ClPhO		**28**, 73
8	PhS		**29**, 87
10	PhO	**24**, 3	**30**, 87
11	4-ClPhO	**25**, 3	**31**, 76
12	PhS	**22**, 30	**32**, 20
13	NMe_2	**26**, 22	**33**, 33



Scheme 6



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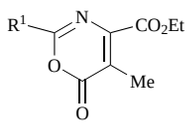
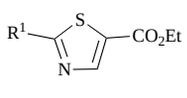
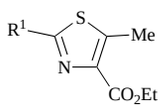


22 R^1 = SPh
23 R^1 = Ph
24 R^1 = OPh
25 R^1 = 4-ClPhO
26 R^1 = NMe_2



27 R^1 = OPh
28 R^1 = 4-ClPhO
29 R^1 = SPh



30 R^1 = OPh
31 R^1 = 4-ClPhO
32 R^1 = SPh
33 R^1 = NMe_2

obtained from isoxazolone **4** proceeded smoothly, allowing the isolation of the corresponding thiazoles **27**–**29** in 65–87% yield respectively. However, the photolysis of the thioacyl derivatives **10**–**13** derived from isoxazolone **15**, gave yields of the thiazole **30**–**33** varying from 33–87%, but accompanied by 3–30% yields of the corresponding 1,3-oxazin-6-ones **22**, **24**, **25** and **26**. These results suggest that the electron withdrawing effects of the 4-ethoxycarbonyl group and the 2-thioacyl group leads to rapid formation of the carbene precursor of the thiazole, and that the isoxazole–nitrone isomerisation is facilitated by the 3-ethoxycarbonyl group, with subsequent reaction of the nitrone with the thiocarbonyl group, ultimately leading to 1,3-oxazin-6-one formation. The above results show that the elimination of sulfur is both a thermal and a photochemical process.

In conclusion, the reaction of 5-oxo-2,5-dihydroisoxazoles with thiocarbonyl chlorides gives *N*-thioacylisoxazolones which upon photolysis afford thiazoles and 1,3-oxazin-6-ones in good to excellent overall yields.

Experimental

General experimental procedures have been described previously.[3] All commercially available thiocarbonyl chlorides were purchased either from the Sigma/Aldrich Chemical Company or Merck Chemicals. The thioacylated isoxazolones were not further purified due to their sensitivity towards moisture and light, except where stated. Photolysis was conducted in Pyrex tubes placed in a Rayonet photochemical reactor at 300 nm using purified solvents. Light petroleum refers to the fraction with bp 50–60 °C. *J* Values are given in Hz.

N-Thioacylation of 5-oxo-2,5-dihydroisoxazoles

Ethyl 5-oxo-2-phenoxythiocarbonyl-2,5-dihydroisoxazole-4-carboxylate 6. Ethyl 5-oxo-2,5-dihydroisoxazole-4-carboxylate **4**[24] (100 mg, 0.637 mmol) was dissolved in anhydrous benzene (20 ml) and pyridine (57 µl, 0.701 mmol) under an atmosphere of nitrogen. The mixture was stirred in the dark after the addition of phenylthiocarbonyl chloride (97 µl, 0.701 mmol). After 24 h the solvent was removed and the residue diluted with dichloromethane–diethyl ether (1:4) (20 ml) and washed with water (20 ml). The organic layer was dried (Na_2SO_4) and evaporated, affording the title compound as a yellow solid (near quantitative), which was recrystallised from dichloromethane–diethyl ether–light petroleum as *pale yellow needles*, mp 108–111 °C (near quantitative) (Found: $M^+ - CO_2$, 249.0461. $C_{12}H_{11}NO_3S$ requires *M*, 249.0460); δ_H 1.37 (3H, t, *J* 7.1), 4.36 (2H, q, *J* 7.14), 7.12–7.18 (2H, m), 7.32–7.39 (1H, m), 7.42–7.51 (2H, m), 9.29 (1H, s); δ_C 14.1, 61.6, 101.9, 121.4, 127.4, 129.7, 147.3, 152.1, 159.5, 161.6, 175.7; ν_{max}/cm^{-1} 1799, 1712, 1592, 1460; *m/z* 249 (M − 44, 2%), 202 (21), 168 (32), 137 (35), 109 (41), 94 (24).

The following compounds were prepared by the above method.

Ethyl 2-(4-chlorophenoxythiocarbonyl)-5-oxo-2,5-dihydroisoxazole-4-carboxylate 7. After 4 h at room temperature the title compound was obtained as a yellow solid (near quantitative), which was recrystallised from dichloromethane–diethyl ether–light petroleum as *pale yellow needles*, mp 105 °C (Found: $M^+ - CO_2$, 283.0063. $C_{12}H_{10}{}^{35}ClNO_3S$ requires *M*, 283.0070); δ_H 1.36 (3H, t, *J* 7.1), 4.35 (2H, q, *J* 7.1), 7.1–7.3 (2H, m), 7.4–7.55 (2H, m), 9.26 (1H, s); δ_C 14.0, 61.6, 102.1, 123.0, 129.8, 132.9, 147.2, 150.4, 159.3, 161.5, 175.2; ν_{max}/cm^{-1} 1805, 1716, 1594, 1485; *m/z* 283 (M − 44, 3%), 270 (11), 237 (6), 205 (6), 171 (14), 143 (39), 128 (100).

Ethyl 5-oxo-2-phenylsulfanylthiocarbonyl-2,5-dihydroisoxazole-4-carboxylate 8. After 24 h at room temperature the title compound was obtained as a yellow solid (85%) which was recrystallised from diethyl ether–light petroleum affording *yellow needles*, mp 112–114 °C (Found: M^+, 309.0159. $C_{13}H_{11}NO_4S_2$ requires *M*, 309.0130); δ_H 1.36 (3H, t, *J* 7.1), 4.36 (2H, q, *J* 7.1), 7.45–7.61 (5H, m), 9.33 (1H, s); δ_C 14.0, 61.5, 101.8, 127.1, 129.8, 131.2, 135.9, 145.2, 159.6, 161.4, 190.4; ν_{max}/cm^{-1} 1805, 1707, 1588, 1463; *m/z* 309 (M, 6%), 277 (3), 218 (22), 168 (100), 153 (88), 140 (31).

Ethyl 2-dimethylaminothiocarbonyl-5-oxo-2,5-dihydroisoxazole-4-carboxylate 9. After 48 h at room temperature a 1:1 mixture of the title compound and ethyl 5-dimethylaminothiocarbonyloxyisoxazole-4-carboxylate **16** was obtained as a yellow oil. On standing for 5 days in deuteriochloroform (0.5 ml) isomerisation occurred allowing the isolation of a mixture of the *title compound* (36%) and *O*-acylated product **16** (6%); **9**: (Found: M^+, 244.0497. $C_9H_{12}N_2O_4S$ requires *M*, 244.0518); δ_H 1.36 (3H, t, *J* 7.1), 3.49 (3H, s), 3.52 (3H, s), 4.34 (2H, q, *J* 7.1), 9.32 (1H, s); δ_C 14.2, 44.8, 45.5, 61.2, 98.1, 152.6, 160.0, 163.2, 172.9; ν_{max}/cm^{-1} 1805, 1713, 1575; *m/z* 244 (M, 1%), 200 (9), 156 (6), 123 (22), 112 (6), 88 (97). Repetition of the reaction at reflux (2 h) gave a mixture of unidentified products (100 mg) which later decomposed.

After refluxing a 4:1 mixture (57 mg) of the above acylated

products for 1 h in anhydrous benzene (10 ml), radial chromatography (diethyl ether–light petroleum, 4:1) gave two fractions. The first, obtained as a colourless oil, was identified as *ethyl* 5-*dimethylaminoisoxazole*-4-*carboxylate* **18** (21 mg, 95% based on initial *O*-acylated material) (Found: M^+, 184.0842. $C_8H_{12}N_2O_3$ requires *M*, 184.0848); δ_H 1.35 (3H, t, *J* 7.1), 3.09 (6H, br d), 4.33 (2H, q, *J* 7.1), 8.65 (1H, s); δ_C 14.2, 37.4, 61.3, 117.7, 151.1, 160.2, 164.0; ν_{max}/cm^{-1} 1699, 1583, 1455; *m/z* 184 (M, 4%), 157 (1), 155 (1), 113 (3), 111 (2), 86 (17), 83 (3).

The second, obtained as a pale yellow oil, was identified as *ethyl* 2-*dimethylamino*-6-*oxo*-6H-1,3-*oxazine*-5-*carboxylate* **20** (11 mg, 92% based on *N*-acylated material) (Found: M^+, 212.0793. $C_9H_{12}N_2O_4$ requires *M*, 212.0797); δ_H 1.36 (3H, t, *J* 7.1), 3.43 (6H, s), 4.35 (2H, q, *J* 7.1), 9.34 (1H, s); δ_C 14.3, 44.4, 61.4, 98.4, 142.8, 160.2, 163.3, 173.1; *m/z* 212 (M, 7%), 184 (8), 155 (18), 140 (7).

When isoxazolone **4** was reacted with dimethylcarbamoyl chloride in anhydrous pyridine–benzene as above, but at 80 °C for 3 h, the crude product now contained three products (^1H, ^{13}C NMR analysis). The major product was assumed to be the malonate **17** on the basis of its spectral properties (Found: M^+, 218.0718. $C_8H_{14}N_2O_3S$ requires *M*, 218.0725); δ_H 1.32 (3H, t, *J* 7.2), 3.486 (2H, s), 3.491 (3H, s), 3.51 (3H, s), 4.27 (2H, q, *J* 7.2); δ_C 13.8, 24.6, 44.8, 45.5, 62.8, 160.0, 160.0, 162.9.

Reaction of thiobenzoyl chloride[8,25] with 4. After 15 h at room temperature ethyl 6-oxo-2-phenyl-6*H*-1,3-oxazine-5-carboxylate **21** was obtained as a red–brown solid (90%), which was recrystallised from dichloromethane–light petroleum as *white needles*, mp 112–114 °C (Found: M^+, 245.0685. $C_{13}H_{11}NO_4$ requires *M*, 245.0688); δ_H 1.39 (3H, t, *J* 7.1), 4.39 (2H, q, *J* 7.1), 7.47–7.55 (2H, m), 7.61–7.68 (1H, m), 8.23–8.29 (2H, m), 8.59 (1H, s); δ_C 14.1, 61.6, 111.7, 128.7, 128.9, 129.3, 134.5, 154.0, 160.5, 162.0, 168.0; ν_{max}/cm^{-1} 1786, 1709, 1604, 1519; *m/z* 245 (M, 9%), 188 (2), 160 (2), 121 (3), 105 (100).

Ethyl 4-methyl-5-oxo-2-phenoxythiocarbonyl-2,5-dihydroisoxazole-3-carboxylate 10. After 2 h reflux the title compound was obtained as a *yellow oil* (near quantitative) (Found: $M^+ - S$, 275.0784. $C_{14}H_{13}NO_5$ requires *M*, 275.0794); δ_H 1.34 (3H, t, *J* 7.1), 2.02 (3H, s), 4.39 (2H, q, *J* 7.1), 7.09–7.15 (2H, m), 7.29–7.36 (1H, m), 7.40–7.48 (2H, m); δ_C 7.2, 13.7, 63.5, 110.7, 121.7, 127.2, 129.7, 145.5, 152.2, 158.4, 166.2, 177.4; ν_{max}/cm^{-1} 1781, 1743, 1636, 1591; *m/z* 307 (M, 1%), 275 (1), 263 (12), 217 (8), 205 (7), 189 (7), 182 (26), 154 (10), 137 (22), 109 (13).

Ethyl 2-(4-chlorophenoxythiocarbonyl)-4-methyl-5-oxo-2,5-dihydroisoxazole-3-carboxylate 11. After 3 h at room temperature the title compound was obtained as a yellow solid (98%), which was recrystallised from diethyl ether–light petroleum as *white needles*, mp 83–85 °C (Found: $M^+ - CO_2$, 297.0223. $C_{13}H_{12}{}^{35}ClNO_3S$ requires *M*, 297.0226); δ_H 1.35 (3H, t, *J* 7.1), 2.03 (3H, s), 4.40 (2H, q, *J* 7.1), 7.08–7.2 (2H, m), 7.40–7.52 (2H, m); δ_C 7.2, 13.7, 63.5, 111.1, 123.3, 129.8, 132.7, 145.4, 150.5, 158.3, 166.0, 176.9; ν_{max}/cm^{-1} 1783, 1742, 1633; *m/z* 297 (M − 44, 7%), 251 (2), 182 (19), 128 (28).

Ethyl 4-methyl-5-oxo-2-phenylsulfanylthiocarbonyl-2,5-dihydroisoxazole-3-carboxylate 12. After 20 h at room temperature a mixture of the title compound (43%) and ethyl 4-methyl-5-phenylsulfanylthiocarbonyloxyisoxazole-3-carboxylate **14** (57%) were obtained as a yellow oil. Compound **12** (Found: $M^+ - S$, 291.0583. $C_{14}H_{13}NO_4S$ requires *M*, 291.0565); δ_H 1.31 (3H, t, *J* 7.1), 1.97 (3H, s), 4.32 (2H, q, *J* 7.1), 7.38–7.52 (3H, m), 7.57–7.62 (2H, m); δ_C 6.9, 13.5, 62.4, 110.3, 127.8, 129.4, 130.9, 135.0, 145.6, 160.0, 167.0, 190.3; ν_{max}/cm^{-1} (mixture) 1760, 1601, 1538; *m/z* 291 (M − 32, 11%), 255 (9), 182 (100), 154 (31), 109 (52). Compound **14**: δ_H 1.31 (3H, t, *J* 7.1), 2.17 (3H, s), 4.29 (2H, q, *J* 7.1), 7.38–7.52 (3H, m), 7.57–7.62 (2H, m); δ_C 11.7, 13.9, 62.0, 117.5, 125.2, 129.5, 130.2, 136.4, 148.2, 158.4, 163.5, 165.5.

Carrying out the above reaction under reflux for 2 h gave an oil which was purified by radial chromatography (diethyl ether–light petroleum, 35:65) on silica, yielding a pale yellow oil which solidified on standing. Recrystallisation from diethyl ether–light petroleum afforded *ethyl* 5-*methyl*-6-*oxo*-2-*phenylsulfanyl*-6H-1,3-*oxazine*-4-*carboxylate* **22** (84%) as colourless cubes, mp 61–62 °C (Found: C, 58.0; H, 4.4; N, 4.7%; M^+, 291.0557. $C_{14}H_{13}NO_4S$ requires C, 57.7; H, 4.5; N, 4.8%; *M*, 291.0565); δ_H 1.32 (3H, t, *J* 7.1), 2.17 (3H, s), 4.31 (2H, q, *J* 7.1), 7.4–7.47 (3H, m), 7.59–7.62 (2H, m); δ_C 11.8, 13.9, 62.1, 117.6, 125.3, 129.4, 130.3, 135.1, 148.3, 160.1, 163.6, 167.1; ν_{max}/cm^{-1} 1755, 1600, 1537; *m/z* 291 (M, 8%), 246 (1), 182 (100), 154 (38), 126 (7), 109 (32), 82 (26).

Ethyl 2-dimethylaminothiocarbonyl-4-methyl-5-oxo-2,5-dihydroisoxazole-3-carboxylate 13. After 2 h at reflux, a mixture of the title compound (69%) and ethyl 4-methyl-5-dimethylaminothiocarbamoyloxyisoxazole-3-carboxylate **15** (19%) was isolated as a yellow oil which could not be further purified. Compound **13** (Found: M^+, 258.0669. $C_{10}H_{14}N_2O_4S$ requires *M*, 258.0674); δ_H 1.31 (3H, t, *J* 7.1), 2.08 (3H, s), 3.43 (6H, br s), 4.32 (2H, q, *J* 7.1); δ_C 7.2, 12.9, 43.9, 44.6, 61.5, 113.6, 150.4, 157.6, 168.9, 179.8; ν_{max}/cm^{-1} (mixture) 1770, 1732, 1651, 1538; *m/z* 258 (M, 1%), 214 (6), 143 (10), 123 (43), 88 (100). Isoxazole **15**: δ_H 1.34 (3H, t, *J* 7.1), 2.06 (3H, s), 3.44 (3H, s), 3.46 (3H, s), 4.36 (2H, q, *J* 7.1).

Reaction of thiobenzoyl chloride[8,25] with 5. After 24 h at room temperature the residue was subjected to radial chromatography (diethyl ether–light petroleum, 35:65) on silica affording ethyl 5-methyl-6-oxo-2-phenyl-6*H*-1,3-oxazine-4-carboxylate **23** as a pale yellow oil (70%) which was recrystallised from diethyl ether–light petroleum as colourless crystals, mp 100–101 °C (Found: C, 64.9; H, 5.1; N, 5.2%; M^+, 259.0829. $C_{14}H_{13}NO_4$ requires C, 64.9; H, 5.1; N, 5.4%; *M*, 259.0845); δ_H 1.42 (3H, t, *J* 7.1), 2.28 (3H, s), 4.43 (2H, q, *J* 7.1), 7.42–7.50 (2H, m), 7.52–7.58 (1H, m), 8.17–8.22 (2H, m); δ_C 12.1, 14.0, 62.1, 120.6, 128.3, 128.6, 129.2, 133.1, 148.7, 160.5, 160.9, 164.1; ν_{max}/cm^{-1} 1754, 1717, 1615; *m/z* 259 (M, 15%), 213 (11), 201 (2), 185 (8), 159 (2), 121 (20), 105 (100).

Ethyl 2-phenoxythiazole-5-carboxylate 27

The isoxazolone **6** (150 mg) was dissolved in acetone (160 ml) and irradiated through Pyrex for 25 min. Removal of the solvent gave a residue which was subjected to radial chromatography (dichloromethane–diethyl ether–light petroleum, 5:30:65) on silica affording the title compound (83 mg, 65%) as a pale yellow oil, which crystallised on standing as pale yellow transparent platelets, mp 26–30 °C[26] (Found: M^+, 249.0461. Calc. for $C_{12}H_{11}NO_3S$: *M*, 249.0460); δ_H 1.33 (3H, t, *J* 7.12), 4.31 (2H, q, *J* 7.12), 7.26–7.34 (3H, m), 7.4–7.48 (2H, m), 7.90 (1H, s); δ_C 14.2, 61.3, 120.4, 122.9, 126.6, 130.1, 144.5, 154.6, 161.1, 177.4; ν_{max}/cm^{-1} 1713, 1594, 1537, 1450; *m/z* 249 (M, 39%), 221 (9), 204 (13), 177 (8), 149 (10), 121 (7).

The following compounds were prepared by a similar method.

Ethyl 2-(4-chlorophenoxy)thiazole-5-carboxylate 28. After photolysis of **7** for 20 min as above, the residue was subjected to radial chromatography (dichloromethane–diethyl ether–light petroleum, 5:30:65) on silica affording the title compound (73%) as a pale yellow oil, which crystallised on standing as pale yellow transparent platelets and was recrystallised from diethyl ether–light petroleum as white needles, mp 58–62 °C[26] (Found: M^+, 283.0074. Calc. for $C_{12}H_{10}{}^{35}ClNO_3S$: *M*, 283.0070); δ_H 1.35 (3H, t, *J* 7.13), 4.33 (2H, q, *J* 7.13), 7.24 (2H, m), 7.4–7.52 (2H, m), 7.87 (1H, s); δ_C 14.2, 61.4, 121.8, 123.3, 130.1, 131.9, 144.2, 152.9, 161.0, 176.6; ν_{max}/cm^{-1} 1710, 1538, 1486; *m/z* 283 (M, 60%), 238 (29), 220 (52), 148 (24), 138 (100).

Ethyl 2-phenylsulfanylthiazole-5-carboxylate 29. After photolysis of **8** for 25 min the residue was subjected to radial chromatography (dichloromethane–diethyl ether–light petroleum, 5:30:65) on silica affording the title compound as a pale yellow oil (87%)[26] (Found: M^+, 265.0227. Calc. for $C_{12}H_{11}NO_2S_2$: *M*, 265.0231); δ_H 1.31 (3H, t, *J* 7.13), 4.28 (2H, q, *J* 7.12), 7.45–7.53 (3H, m), 7.67–7.71 (2H, m), 8.20 (1H, s); δ_C

14.2, 61.4, 129.0, 129.7, 130.2, 130.7, 135.0, 148.8, 160.7, 175.5; ν_{max}/cm^{-1} 1713, 1582, 1516; *m/z* 265 (M, 31%), 236 (33), 218 (23), 192 (21), 153 (23), 141 (50), 123 (16), 109 (100).

Ethyl 2-phenoxy-5-methylthiazole-4-carboxylate 30. After photolysis of **10** for 30 min, the residue was subjected to radial chromatography (dichloromethane–diethyl ether–light petroleum, 5:30:65) on silica affording the title compound (87%) and ethyl 5-methyl-6-oxo-2-phenoxy-6*H*-1,3-oxazine-4-carboxylate **24** (3%) as a pale yellow oil (Found: M$^+$, 275.0780. $C_{14}H_{13}NO_5$ requires *M*, 275.0794). Kugelrohr distillation (150–170 °C/0.01 mmHg) gave the pure title compound[26] (Found: M$^+$, 263.0621. Calc. for $C_{13}H_{13}NO_3S$: *M*, 263.0616); δ_H 1.38 (3H, t, *J* 7.13), 2.65 (3H, s), 4.36 (2H, q, *J* 7.13), 7.21–7.28 (3H, m), 7.36–7.43 (2H, m); δ_C 13.0, 14.2, 60.9, 119.7, 125.9, 129.9, 135.7, 138.9, 155.3, 162.0, 167.9; ν_{max}/cm^{-1} 1712, 1629, 1530, 1488; *m/z* 263 (M, 56%), 217 (50), 189 (54), 137 (57), 109 (17).

Ethyl 2-(4-chlorophenoxy)-5-methylthiazole-4-carboxylate 31. After photolysis of **11** for 30 min, the residue was subjected to radial chromatography (dichloromethane–diethyl ether–light petroleum, 5:30:65) on silica affording the title compound (76%) and ethyl 2-(4-chlorophenoxy)-5-methyl-6-oxo-6*H*-1,3-oxazine-4-carboxylate **25** (3%) as a pale yellow oil (Found: M$^+$, 309.0379. $C_{14}H_{12}{}^{35}ClNO_5$ requires *M*, 309.0404). The oil solidified on standing and was recrystallised from diethyl ether–light petroleum to afford the title compound as *white needles*, mp 58–60 °C (Found: M$^+$, 297.0222. $C_{13}H_{12}{}^{35}ClNO_3S$ requires *M*, 297.0226); δ_H 1.36 (3H, t, *J* 7.12), 2.64 (3H, s), 4.34 (2H, q, *J* 7.12), 7.2–7.33 (2H, m), 7.33 (2H, m); δ_C 13.1, 14.3, 61.0, 121.0, 129.9, 131.0, 135.8, 139.3, 153.7, 162.0, 167.0; ν_{max}/cm^{-1} 1706, 1524, 1484; *m/z* 297 (M, 88%), 251 (96), 223 (85), 171 (71), 139 (31), 111 (100).

Photolysis of ethyl 4-methyl-5-oxo-2-phenylsulfanylthiocarbonyl-2,5-dihydroisoxazole-3-carboxylate 12

A 43:57 mixture of *N*- and *O*-acylated compounds, **12** and **14** from above (190 mg), was irradiated for 105 min. The crude product was subjected to Kugelrohr distillation (150–170 °C/0.01 mmHg) but still contained four products (119 mg). The mixture was subsequently separated by radial chromatography (diethyl ether–light petroleum, 1:3) into three fractions: the first was identified as diphenyl disulfide (11 mg), the second decomposed and was unidentified (24 mg). The third, a pale yellow oil, was a mixture of ethyl 5-methyl-2-phenylsulfanylthiazole-4-carboxylate **32** (32 mg, 20% overall) and ethyl 5-methyl-6-oxo-2-phenylsulfanyl-6*H*-1,3-oxazine-4-carboxylate **22** (52 mg, 30% overall). *Ethyl 5-methyl-2-phenylsulfanylthiazole-4-carboxylate*, **32** (Found: M$^+$, 279.0391. $C_{13}H_{13}NO_2S_2$ requires *M*, 279.0388); δ_H 1.40 (3H, t, *J* 7.12), 2.63 (3H, s), 4.40 (2H, q, *J* 7.12), 7.40–7.47 (3H, m), 7.58–7.65 (2H, m); *ethyl 5-methyl-6-oxo-2-phenylsulfanyl-6H-1,3-oxazine-4-carboxylate*, **22** (Found: M$^+$, 291.0566. $C_{14}H_{13}NO_4S$ requires *M*, 291.0565).

Photolysis of ethyl 2-dimethylaminothiocarbonyl-4-methyl-5-oxo-2,5-dihydroisoxazole-3-carboxylate 13

After 1.5 h the residue from photolysis of a 3:1 mixture of *N*- and *O*-acylated isoxazolones, **13** and **15**, was subjected to Kugelrohr distillation (150–170 °C/0.1 mmHg) affording a yellow oil which was subjected to radial chromatography (diethyl ether–light petroleum, 1:4). Two fractions were collected. The first contained *ethyl 2-dimethylamino-5-methyl-6-oxo-6H-1,3-oxazine-4-carboxylate* **26** (22%) (Found: M$^+$, 226.0962. $C_{10}H_{14}N_2O_4$ requires *M*, 226.0954); δ_H 1.42 (3H, t, *J* 7.14), 2.07 (3H, s), 3.37 (3H, s), 3.44 (3H, s), 4.44 (2H, q, *J* 7.14); δ_C 6.7, 14.1, 39.3, 43.8, 61.9, 102.6, 156.5, 160.2, 165.2, 182.4; ν_{max}/cm^{-1} 1738, 1733, 1656, 1652, 1563; *m/z* 226 (M, 3%), 180 (4), 169 (4), 154 (7), 140 (6), 124 (3), 88 (15).

The second fraction contained *ethyl 2-dimethylamino-5-methylthiazole-4-carboxylate* **33** (33%) (Found: M$^+$, 214.0777. $C_9H_{14}N_2O_2S$ requires *M*, 214.0776); δ_H 1.39 (3H, t, *J* 7.12), 2.59 (3H, s), 3.07 (6H, s), 4.35 (2H, q, *J* 7.12); δ_C 12.8, 14.4, 40.1, 60.8, 132.9, 138.0, 163.0, 166.4; ν_{max}/cm^{-1} 1712, 1703, 1698, 1574; *m/z* 214 (M, 41%), 185 (10), 168 (21), 153 (15), 140 (57), 126 (5), 88 (100).

Crystal structure analysis†

X-Ray crystallographic analysis of compound 23. $C_{14}H_{13}NO_4$, $M = 259.26$, orthorhombic, space group *Pbca*, $a = 8.199(2)$, $b = 17.364(2)$, $c = 18.097(2)$ Å, $U = 2576.4(2)$ Å^3, $Z = 8$, $D_c = 1.337$ Mg m^{-3}, Mo-Kα radiation, $\lambda = 0.710\,73$ Å, $T = 293$ K, $\mu = 0.10$ mm^{-1}, $F(000) = 1088$, crystal dimensions 0.60 × 0.10 × 0.10 mm. Unit cell dimensions determined from 25 centred reflections with $11.3 < 2\theta < 15.0°$. Data were measured on a Nonius CAD-4/PC diffractometer with graphite-monochromated Mo-Kα radiation using ω–2θ scans. 4946 Reflections were measured over the range $2\theta < 25°$ with $-9 < h < 9$, $0 < k < 20$, $0 < l < 21$ reflections measured every 7200 s of exposure time showing an intensity variation of ±0.5%. The reflections were corrected for absorption by Gaussian quadrature from the crystal shape ($T_{min} = 0.986$, $T_{max} = 0.990$) and for Lorentz and polarisation effects. They were merged to give 2266 independent reflections ($R_{int} = 0.0215$) with $F^2 > 0$. The structure was solved by direct methods. All crystallographic calculations were done with the XTAL3.4 system of programs.[27] Hydrogen atoms were placed in calculated positions (C–H = 0.95 Å) with fixed isotropic displacement parameters. All non-hydrogen atoms were refined with anisotropic displacement parameters using the full matrix based on F^2, giving $R(F) = 0.064$, $wR(F^2) = 0.115$ [$w = 1/\sigma^2(F^2)$], $S = 1.22(3)$, $(\Delta/\sigma)_{max} = 0.0038$ for 173 parameters and 1078 reflections with $F^2 > 1.3\sigma(F^2)$. An extinction parameter[28] was refined, $g = 2.4(3) \times 10^4$. The crystal was weakly diffracting and the $1.3\sigma(F^2)$ cut-off was chosen to include enough reflections in the refinement to give an acceptable observation/parameter ratio, but to exclude the very weak data. The maximum and minimum residual densities in the final $\Delta\rho$ map were 0.29 and −0.32 e Å^{-3}, respectively.

X-Ray crystallographic analysis of compound 22. $C_{14}H_{13}NO_4S$, $M = 291.32$, triclinic, space group $P\bar{1}$, $a = 7.986(1)$, $b = 9.281(2)$, $c = 9.686(1)$ Å, $\alpha = 94.05(1)$, $\beta = 95.70(1)$, $\gamma = 100.71(1)°$, $U = 698.0(2)$ Å^3, $Z = 2$, $D_c = 1.384$ Mg m^{-3}, Mo-Kα radiation, $\lambda = 0.710\,73$ Å, $T = 293$ K, $\mu = 0.24$ mm^{-1}, $F(000) = 304$, crystal dimensions 0.46 × 0.40 × 0.21 mm. Unit cell dimensions determined from 25 centred reflections with $18.3 < 2\theta < 23.2°$. Data were measured on a Nonius CAD-4/PC diffractometer with graphite-monochromated Mo-Kα radiation using ω–2θ scans. 5030 Reflections were measured over the range $2\theta < 25°$ with $-9 < h < 9$, $-11 < k < 11$, $-11 < l < 11$. 3 reflections measured every 7200 s of exposure time, showing an intensity variation of ±0.5%. The reflections were corrected for absorption by Gaussian quadrature from the crystal shape ($T_{min} = 0.910$, $T_{max} = 0.953$) and for Lorentz and polarisation effects. They were merged to give 2548 independent reflections ($R_{int} = 0.011$) with $F^2 > 0$. The structure was solved by direct methods. All crystallographic calculations were done with the XTAL3.4 system of programs.[27] Hydrogen atoms were placed in calculated positions (C–H = 0.95 Å). All non-hydrogen atoms were refined with anisotropic displacement parameters and hydrogen atoms with isotropic displacement parameters using the full matrix based on F^2, giving $R(F) = 0.051$, $wR(F^2) = 0.104$ [$w = 1/\sigma^2(F^2)$], $S = 1.24(2)$, $(\Delta/\sigma)_{max} = 0.001$ for 233 parameters and 2548 reflections with $F^2 > 0$. The maximum and minimum residual densities in the final $\Delta\rho$ map were 0.34 and −0.30 e Å^{-3}, respectively.

† Atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/117.

Acknowledgements

The authors are grateful for support from the Australian Research Council. C. M. W. acknowledges an Australian Postgraduate Award.

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Paper 7/00646B
Received 28*th January* 1997
Accepted 20*th March* 1997

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