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Pseudohalogen Chemistry. XI.[1] Some Aspects of the Chemistry of α-Thiocyanato-β-Dicarbonyl Compounds

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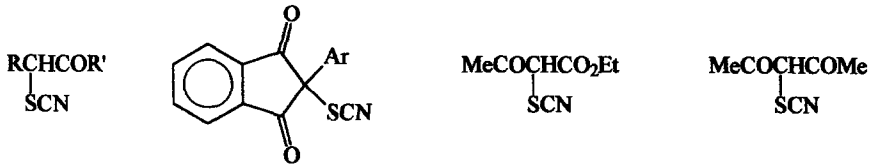
Abstract: Enolised α-thiocyanato-β-dicarbonyl compounds dimerise in ethanol at room temperature to give tautomeric 4,5-disubstituted 2-amino- and 2-acetamido-thiazoles by a C-S-C + C-N cyclisation. Tautomerism is due to the unusual 4-(β-dicarbonyl-α-thio) substituent. Competing intramolecular cyclisations lead to minor amounts of heterocycles containing the thiazole and /or oxathiole ring systems.

INTRODUCTION

α-Thiocyanatocarbonyl compounds (1) are readily prepared from the corresponding halides and a metal thiocyanate in organic or aqueous organic solvents.[2] There are only a few reports of the extension of this reaction to β-dicarbonyl systems and these suggest that the reaction proceeds along two different pathways. Thus, a series of stable 2-thiocyanatoindan-1,3-diones (2) has been prepared and characterised,[3] whereas attempts to prepare ethyl 2-thiocyanatoacetoacetate (3)[4,5,6] and 3-thiocyanatopentane-2,4-dione (4)[5] led to compounds whose structures have remained unknown since Hantzsch's original investigations in 1887.[4]



1 2 3 4

We have re-investigated these reactions using diethyl malonate, acetoacetic ester and acetylacetone systems as models, and now report our results and interpretations.[7]

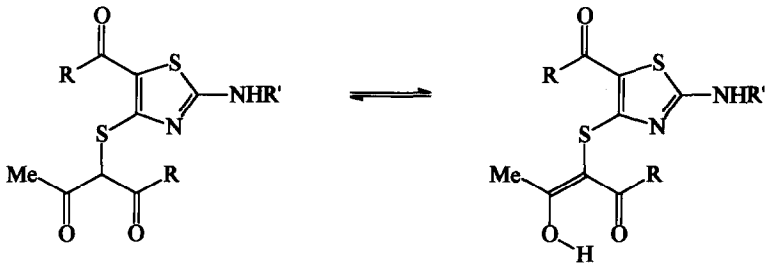
RESULTS AND DISCUSSION

Treatment of diethyl chloromalonate and ethyl 2-chloro-2-methylacetoacetate with potassium or ammonium thiocyanate in ethanol led smoothly to the expected thiocyanates 5 and 6.[2]

5 6

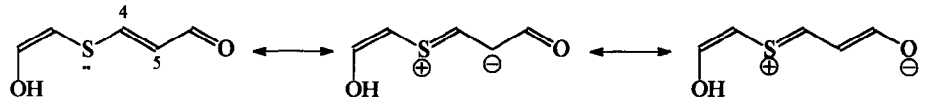
Under the same conditions, methyl 2-chloroacetoacetate, ethyl 2-chloroacetoacetate and 3-chloropentan-2,4-dione reacted to give, in each case, one major product and four minor products (TLC), none of which was a thiocyanate (IR). By carrying out the reactions in acetone at 0°C, it was possible to isolate the thiocyanate **4** (but not **3** or its methyl analogue) as an unstable solid which , on exposure to the normal reaction conditions, gave the same mixture of major and minor products as before.

Major Products. The major products from methyl 2-chloroacetoacetate, ethyl 2-chloroacetoacetate and 3-chloropentane-2,4-dione were isolated by chromatography and/or recrystallisation in 52%, 62% and 44% yield respectively. Elemental analysis and high-resolution mass spectrometry gave the respective molecular formulae as $C_{10}H_{12}O_5N_2S_2$, $C_{12}H_{16}O_5N_2S_2$ and $C_{10}H_{12}O_3N_2S_2$, indicating that extensive but common molecular change had occurred and that each product has six double-bond equivalents. Spectroscopic analysis, aided by the spectra of simple model compounds (see Experimental), showed that the products have the 4,5-disubstituted 2-aminothiazole[8] structure **7** (R' = H) which has the novel tautomeric β-dicarbonyl-α-thio substituent at C-4.



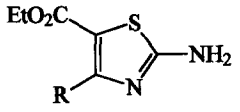
7a **7b**

The spectra of the products from the β-ketoester systems show that they exist as mixtures of the keto and enol tautomers **7a** and **7b** (R = OMe, OEt; R' = H). For example, **7** (R = OEt; R' = H) shows in its IR spectrum three N-H stretching bands between 3425 $cm^{-1}$and 3210 cm^{-1}, three carbonyl stretching bands in the 1735-1642 cm^{-1} region, and a band at 1615 cm^{-1} due to enolic C=C stretching and/or N-H bending. Its 270 MHz ^1H NMR spectrum in DMSO-d_6 shows four ethyl signals, two methyl singlets, one CH singlet, two NH_2 singlets and an enolic OH singlet. Furthermore, its ^{13}C NMR spectrum shows 24 signals in the regions required by the ring CO_2Et, 2-aminothiazole,[8,9] and tautomeric ethyl acetoacetate[10] fragments. Comparison of its NMR data with those of the parent compounds **8** (R = H) and ethyl acetoacetate shows that the S atom of the 4-(β-dicarbonyl-α-thio) substituent exerts a significant effect on certain chemical shifts due to its ability to act as a conjugative link between the pseudo-aromatic enolic ring and the thiazole ring (and the CO_2Et group at C-5) as shown below in diagrammatic form.

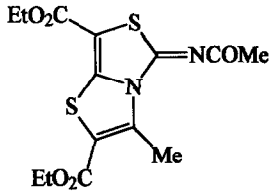


This effect produces shieldings of 11.84 and 12.88 ppm at C-5 of the keto and enol tautomers, and a deshielding of 1.57 ppm at the enolic OH. Similar electron withdrawal from the enolic ring by other α-RS groups, resulting in downfield OH shifts, has been noted elsewhere.[11] The extra delocalisation afforded by the linking S atom is also reflected in the UV spectrum of **7** (R = OEt; R' = H) which shows bands at 322 nm and 266 nm, the former being attributed to the 2-aminothiazole ring [8] and the latter to the keto-enol side chain.[12] Comparison with the UV spectra of the parent compounds **8** (R = H) and ethyl acetoacetate shows that the sulphide linkage produces bathochromic shifts of 23 nm in the thiazole absorption and 21 nm in the side-chain absorption.

Confirmation of structure **7** was also provided by several chemical reactions. Thus, **7** (R = OEt; R' = H) was (a) desulphurised by Raney nickel to the known ethyl 2-aminothiazole-5-carboxylate **8** (R = H), (b) decarbethoxylated by sodium chloride in aqueous dimethyl sulphoxide to the ketosulphide **8** (R = SCH_2COMe), and (c) acetylated by acetic anhydride to the amide **7** (R = OEt; R' = COMe); under vigorous acidic conditions, cyclisation to the imide **9** occurred.



8



9

Keto-enol equilibrium data for **7** (R = OMe, OEt; R' = H) in various solvents and at different temperatures are shown in Table 1. These values, and the derived thermodynamic parameters for **7** (R = OMe; R' = H) in DMSO-d_6 solvent, *viz.* ΔG^o = 1220 $Jmol^{-1}$, ΔS^o = -15.3 $Jmol^{-1}K^{-1}$ and ΔH^o = -5890 $Jmol^{-1}$, are similar to those reported for other β-dicarbonyl systems containing electron-withdrawing α-substituents.[13]

Table 1. Keto-Enol Equilibrium Constants (K = [enol]/[keto]) for Compounds **7**

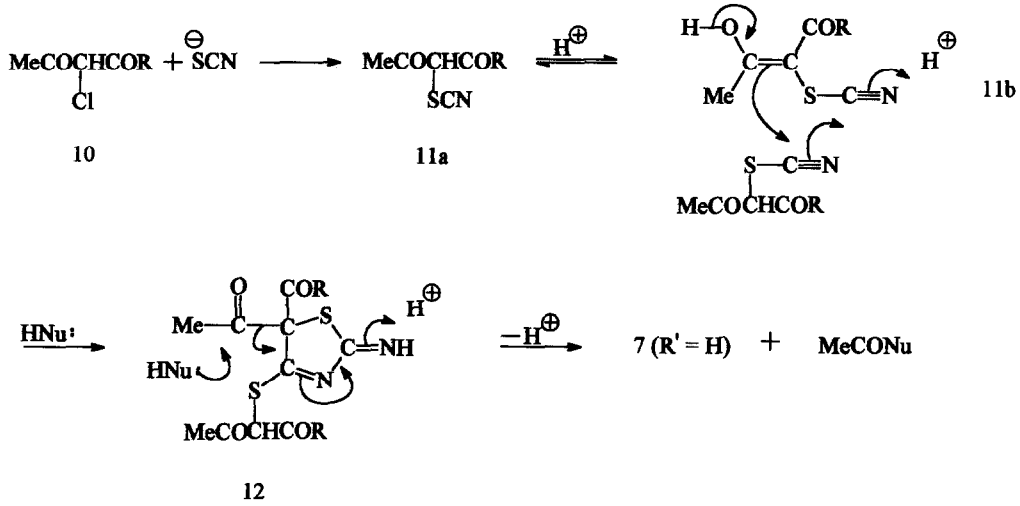
R	R'	Solvent	Temp(°C)	% Enol	K
OMe	H	DMSO-d_6	25	33	0.49
OMe	H	DMSO-d_6	50	30	0.43
OMe	H	DMSO-d_6	75	27	0.37
OMe	H	DMSO-d_6	100	24	0.32
OMe	H	CD_3CN	24	42	0.72
OMe	H	CD_3COCD_3	24	49	0.96
OMe	H	$CDCl_3$	24	67	2.03
OMe	H	C_6D_6	24	87	6.69
OEt	H	DMSO-d_6	24	35	0.54
OEt	H	$CDCl_3$	24	68	2.13
OEt	H	C_6D_6	24	80	4.00
OEt	COMe	DMSO-d_6	24	55	1.22
OEt	COMe	$CDCl_3$	24	75	3.00

The spectral data for the β-diketone system, however, show that the product exists solely in the enol form **7b** (R = Me; R' = H) (see Experimental). Similar behaviour has been noted in many other keto-enol systems and attributed to differences in the strength of the hydrogen bond in **7b**;[11,13] in agreement with this, the NMR signals for the enolic hydrogens in the β-ketoester systems **7** (R = OMe,OEt; R' = H) appear at δ13.55 and δ13.64 respectively in DMSO-d_6 while that for the β-diketone system **7** (R = Me; R' = H) appears at δ17.15. No evidence was found for amino-imino tautomerism, in agreement with other studies on 2-aminothiazoles.[9]

Formation of **7** is rationalised by the mechanism shown in Scheme 1. Like its chloro-precursor **10**, the labile α-thiocyanato-β-dicarbonyl compound **11** formed in the primary nucleophilic substitution reaction is extensively enolised[11] and thus highly nucleophilic. Consequently, the enolic tautomer **11b** undergoes ready cyclodimerisation to the 2-imino-Δ^3-thiazoline **12** through intermolecular nucleophilic addition to an SCN group[2] and a favourable 5-*exo-dig* ring closure[14] involving the second SCN group. Consistent with this proposal, non-enolisable α-thiocyanato-β-dicarbonyl compounds, *eg* **2**, **5**, and **6**, do not undergo this cyclodimerisation. Analogous cyclisations involving *exo*-additions to nitriles, also with the formation of C-amino-substituted heterocycles, have been reported.[15,16]

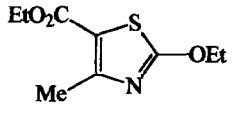
In the final aromatisation step, attack on the acetyl group of **12** by any of the nucleophiles present (see below) leads to de-acetylation and the formation of the 2-aminothiazole **7** (R' = H). The preferential loss of the acetyl group from **12** when R = OMe or OEt is analogous to that found in the Knorr pyrrole synthesis,[17] the Japp-Klingemann reaction,[18] and the synthesis of S-heterocycles from ethyl 2-chloroacetoacetate and potassium cyanodithioimidocarbonate [$(KS)_2CNCN$].[19]

This appears to be the first reported example of a C-S-C + C-N thiazole ring synthesis, which, following the notation used by Sprague and Land,[20] we propose to designate as Type P. It also provides a route to the rather inaccessible 4-RS-thiazoles.[21]



Scheme 1

Minor Products. Examination of the minor products formed in the reactions was restricted mainly to those of the ethyl acetoacetate system. They were separated by chromatography and identified as compounds **7** (R = OEt; R' = COMe), **13**, **14**, and **15** by spectroscopic and chemical methods, again with the aid of simple model compounds. Compound **7** (R = Me; R' = COMe) was isolated from the acetylacetone system.



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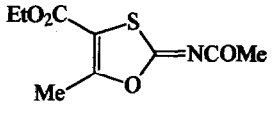
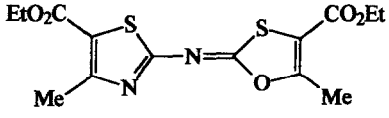


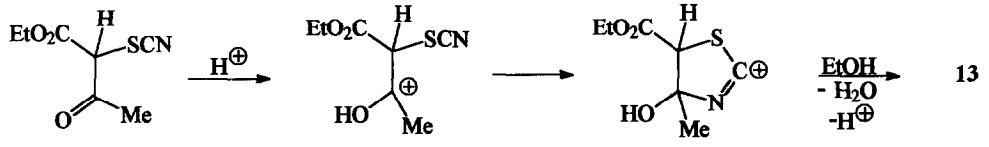
14



15

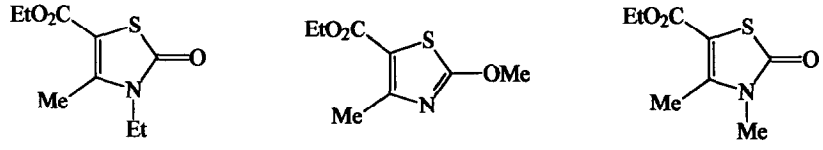
Formation of the amides **7** (R = OEt, Me; R' = COMe) in 5% and 30% yield respectively is attributed to nucleophilic attack on the acetyl group of **12** by the amino group of **7** (R = OEt, Me; R' = H) or by the imino group of another **12** (Scheme 1), and is a further example of acyl transfer from C to N.[22] Amide **7** (R = OEt; R' = COMe) is extensively enolised (Table 1) and **7** (R = Me; R' = COMe) is completely enolised.

Formation of compounds **13, 14** and **15** in 1%, 12% and 1% yield respectively is consistent with the well-established intramolecular cyclisations of α-thiocyanatocarbonyl compounds to thiazoles and oxathioles.[2] Such a pathway to **13**, involving the keto tautomer, is shown in Scheme 2.



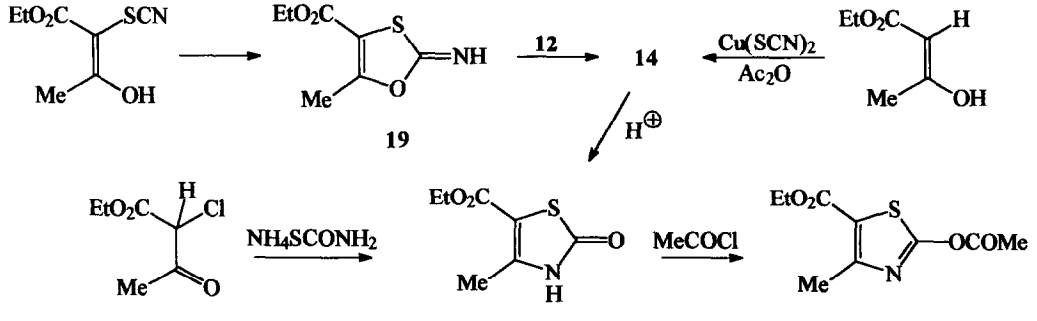
Scheme 2

To confirm that the 2-ethoxythiazole structure **13**, and not the isomeric N-ethylthiazol-2-one structure **16**, is the correct one,[23] the O- and N-methyl analogues **17** and **18** were prepared by unambiguous syntheses.[24] Comparison of the spectral data of the model compounds, especially λ_{max} and δC-2, with those of the reaction product showed clearly that **13** is the correct structure.



16 **17** **18**

Compound **14** arises through cyclisation of the enol tautomer[2] of the thiocyanate to the 2-imino-oxathiole **19**, followed by acyl transfer from **12** (Scheme 3).



Scheme 3

The N-acetyloxathiole[25] structure of **14** was confirmed by an alternative synthesis previously used to prepare N-acetylbenzoxathioles from 2-thiocyanatophenols and copper (II) thiocyanate.[26] Hydrolysis of **14** gave, not the

expected oxathiol-2-one, but the thiazolin-2-one **20**, which was identified by an alternative synthesis using ethyl 2-chloroacetoacetate and ammonium thiocarbamate.[5] Similar ring rearrangements of N-aryloxathiol-2-imines to N-arylthiazolin-2-ones have been reported and the mechanism discussed.[27] Acetylation of **20** gave the 2-O-acetylthiazole **21**, isomeric with **14** (Scheme 3).

In contrast to the other reaction products, compound **15** has both the thiazole and the oxathiole rings present. This is indicated by its pairs of C-4 and C-5 chemical shifts which correspond closely to those of (a) the oxathiole **14** and (b) model thiazoles *eg* the N-acetyl derivative of **8** (R = Me). The formation of **15** is most simply explained by attack of the 2-iminooxathiole **19** on the cyclic carbocation in Scheme 2.

EXPERIMENTAL

General comments. Reactions were monitored on TLC plates of silica gel (Merck 60-F254 or 13181) using CH_2Cl_2/MeOH or $CHCl_3$/MeOH (25:1) as elutant. Components were detected by UV fluorescence, iodine vapour or KIP solution [KI (12 g) and H_2PtCl_6 (1 g) in H_2O (1200 mL)]. Chromatographic separations were carried out using columns of Merck Kieselgel 60 (230-400 mesh). IR spectra were recorded on Perkin-Elmer 197 or Pye-Unicam SP3-100 spectrometers using Nujol mulls for solids and films for liquids; ν_{max} values are given in cm^{-1} units. UV spectra were recorded on Perkin-Elmer 197 or Pye-Unicam SP8-150 spectrometers using ethanol as solvent; λ_{max} values are given in nm units and molar extinction coefficients (ε) are given in m^2mol^{-1} units. Mass spectra (EI) were recorded on VG Micromass 16F or Jeol JMS-DX 303 spectrometers. ^1H and ^{13}C NMR spectra were recorded on Bruker WP 80, Bruker AC 250, Bruker 300, or Jeol JNM-GX spectrometers using TMS as internal standard; in the NMR data given below, s = singlet, d = doublet, t = triplet, q = quartet, ex = exchangeable with D_2O. Melting points (mp) are uncorrected.

Reaction of ethyl 2-chloroacetoacetate with potassium thiocyanate. Ethyl 2-chloroacetoacetate (8.23 g, 0.050 mol) was added to a solution of potassium thiocyanate (5.35 g, 0.055 mol) in ethanol (125 mL) and the mixture was stirred at rt for 3 h. The solvent was removed under reduced pressure and the product extracted with diethyl ether (2 x 75 mL). The ether-insoluble portion consisted of KCl (3.47 g) and a pale yellow solid[4] (0.48 g), mp 260-270° (dec.), which was highly insoluble in the common organic solvents, dilute acids and bases, and was not further examined. The ether-soluble portion was a viscous orange oil (8.64 g) which was separated by flash chromatography (ether / hexane eluant) into the following compounds *a-e*.

a. **Ethyl 2-[2-amino-5-(ethoxycarbonyl)-4-thiazolylthio]acetoacetate [7 (R = OEt; R' = H)].** White prisms (5.16 g, 62%), mp 127-129° (EtOH) (lit.[5] mp 128°). Found: C, 43.49; H, 4.79; N, 8.60; S, 18.82 %. $C_{12}H_{16}O_5N_2S_2$ requires: C, 43.37; H, 4.86; N, 8.43; S, 19.26 %. HRMS (m/z): 332.0499 (M^+); calcd 332.0501. MS (m/z, %): 332, *25* (M^+); 286, *30* (M^+- EtOH); 244, *36* (M^+- EtOH - CH_2CO); 198, *32;* 159, *33;* 43, *100* ($MeCO^+$). IR (ν_{max}): 3425, 3320, 3210 (N-H st); 1735 (C=O st of chain CO_2Et); 1705 (C=O st of COMe); 1642 (C=O st of ring CO_2Et and enolised β-ketoester); 1615 (C=C st / N-H bend). UV (λ_{max} ,ε_{max}); 322, *1495* (thiazole ring); 266, *598* (keto-enol side-chain). ^1H NMR (DMSO-d_6, 270 MHz, δ): 1.24, 1.32, 1.35, 1.36 (4 overlapping t, total 6H, J = 7Hz, OCH_2CH_3 of enol chain, keto chain, ring); 2.22, 2.38 (2 s, total 3H, enol $CH_3C(OH)$, keto CH_3CO); 4.16, 4.17, 4.20, 4.22 (4 overlapping q, total 4H, J = 7Hz, OCH_2CH_3 of enol chain, keto chain, ring); 7.68, 7.78 (2 s, total 2H, ex, NH_2); 5.55, 13.64(2 s, total 1H, ex, keto CH, enol OH). ^{13}C NMR (DMSO-d_6, 67.8 MHz): δ 13.90, 14.10, 14.41, 14.45 (4 OCH_2CH_3); 20.88 (enol $CH_3C(OH)$); 28.54 (keto CH_3CO); 58.64 (keto CHS); 59.87, 60.13, 61.07, 61.99 (4 OCH_2CH_3); 92.44 (enol CS); 102.02, 103.06 (2 C-5); 154.23, 158.68 (2 C-4); 161.64, 161.91 (2 ring CO_2Et); 166.29 (keto CO_2Et); 170.51, 170.78 (2 C-2); 172.45 (enol CO_2Et); 181.95 (enol $CH_3C(OH)$); 199.31 (keto CH_3CO).

b. **Ethyl 2-[2-acetamido-5-(ethoxycarbonyl)-4-thiazolylthio]acetoacetate [7 (R = OEt; R'= COMe)].** Off-white prisms (0.84 g, 9%), mp 116-117° (hexane / CCl_4). Found: C, 41.42; H, 4.40; N, 6.94; S, 15.30 %.

$C_{14}H_{18}N_2O_6S_2 \cdot 0.25\ CCl_4$ requires: C, 41.45; H, 4.39; N, 6.79; S, 15.53 %. MS (m/z, %): 374, *5* (M^+); 328, *10* (M^+- EtOH); 286, *44* (M^+- EtOH - CH_2CO); 244, *18* (M^+-EtOH - 2 CH_2CO); 43, *100* ($MeCO^+$). IR (ν_{max}): 3145 (N-H st); 1740 (C=O st of chain CO_2Et); 1698 (C=O st of chain COMe); 1645 (C=O st of ring CO_2Et and enolised β-keto-ester); 1615 (C=O st of NHCOMe / C=C st / N-H bend). UV (λ_{max} , ε_{max}): 317, *1171* (thiazole ring); 271, *1133* (keto-enol side-chain). ^1H NMR ($CDCl_3$, 80 MHz, δ): 1.20, 1.38 (2 overlapping t, total 6H, J = 7Hz, OCH_2CH_3 of chain, ring); 2.25, 2.28, 2.39 (3 s, total 6H, enol $CH_3C(OH)$, CH_3CONH, keto CH_3CO); 4.20, 4.36 (2 overlapping q, total 4H, J = 7Hz, OCH_2CH_3 of chain, ring); 5.36, 13.72 (2 s, total 1H, ex, keto C*H*, enol O*H*); 8.88, 9.08 (2 broad s, total 1H, ex, enol N*H*, keto N*H*). (In DMSO-d_6 , the N*H* signal is a singlet δ12.52.)

c. **Ethyl 2-ethoxy-4-methylthiazole-5-carboxylate (13)** as white prisms (0.13 g, 1%), mp 41-42° (hexane / ether). Found: C, 50.12; H, 6.19; N, 6.26; S,14.54%. $C_9H_{13}NO_3S$ requires: C, 50.22; H, 6.09; N, 6.51; S, 14.89%. MS (m/z, %): 215, *26* (M^+); 187, *40* (M^+-C_2H_4); 159, 37 (M^+-2 C_2H_4); 57, *100* ($EtCO^+$); 43, *98* ($MeCO^+$). IR (ν_{max}): 1690 (C=O st); 1230, 1075 (ether C-O st). UV (λ_{max} , ε_{max}): 272, *1200*. ^1H NMR (DMSO-d_6, 300 MHz, δ): 1.28, 1.38 (2 t, each 3H, J = 7Hz, OCH_2CH_3, $CO_2CH_2CH_3$); 2.51 (s, 3H, CH_3); 4.24, 4.46(2 q, each 2H, J = 7Hz, OCH_2CH_3, $CO_2CH_2CH_3$). ^{13}C NMR (DMSO-d_6, 75.47 MHz, δ): 13.99 (superimposed OCH_2CH_3, $CO_2CH_2CH_3$); 17.05 (ring CH_3); 60.55 (OCH_2CH_3); 68.26 ($CO_2CH_2CH_3$); 113.06 (*C*-5); 156.12 (*C*-4); 161.25 ($CO_2CH_2CH_3$); 174.34 (*C*-2).

d. **Ethyl N-acetyl-5-methyl-1,3-oxathiol-2-imine-4-carboxylate (14).** White prisms (1.35 g, 12%), mp 67-68° (EtOH / H_2O). Found: C, 47.08; H, 5.00; N, 6.15; S, 13.61%. $C_9H_{11}NO_4S$ requires: C, 47.15; H, 4.84; N, 6.11; S, 13.99%. HRMS (m/z): 229.0399 (M^+); calcd 229.0409. MS (m/z, %): 229, *6* (M^+); 214, *3* (M^+-CH_3); 187, *6* (M^+-CH_2CO); 43, *100* ($MeCO^+$). IR (ν_{max}): 1720 (ester C=O st); 1660 (amide C=O and C=N st). UV (λ_{max} ,ε_{max}): 293, *1029;* 200, *295*. ^1H NMR ($CDCl_3$, 270 MHz, δ): 1.36 (t, 3H, J = 7Hz, CH_2CH_3); 2.37 (s, 3H, ring CH_3); 2.63 (s, 3H, $COCH_3$); 4.34 (q, 2H, J = 7Hz, CH_2CH_3). ^{13}C NMR ($CDCl_3$, 67.8 MHz, δ): 13.72 (CH_2CH_3); 14.13 (ring CH_3); 27.32 ($COCH_3$); 61.97 (CH_2CH_3); 110.03 (*C*-4); 155.18 (*C*-5); 160.55 (CO_2Et); 176.52 (*C*-2); 182.51 (*C*OMe). This compound was also prepared[26] in 42% yield by heating under reflux a stirred mixture of ethyl acetoacetate (3.0 g), cupric thiocyanate (16.4 g), acetic acid (30 mL) and acetic anhydride (30 mL) for 30 min, adding the cooled filtrate to ice-water (500 g), extracting with ether, washing with aqueous $NaHCO_3$, drying (Na_2SO_4), removing the solvent, and purifying the product by chromatography.

e. **Ethyl N-[2-(4-methyl-5-carboxyethylthiazolo)]-5-methyl-1,3-oxathiol-2-imine-4-carboxylate (15).** Pale yellow prisms (0.11 g, 1%), mp 143-144° (MeOH / H_2O). Found: C, 47.42; H, 4.59; N, 7.60%. $C_{14}H_{16}N_2O_6S_2$ requires C, 47.18; H, 4.53; N, 7.86%. HRMS (m/z): 356.0502 (M^+); calcd 356.0501. MS (m/z, %): 356, *100* (M); 328, *8* (M^+- C_2H_4); 311, *20* (M^+- OEt); 284, *16* (M^+- C_2H_4 - CO_2); 213, 25; 71, *20*; 45, *50*. IR (ν_{max}): 1709,1691 (ester C=O st); 1631 (C=N st). UV (λ_{max} ,ε_{max}): 342, *3703*. ^1H NMR ($CDCl_3$, 270 MHz, δ): 1.36, 1.38 (2 overlapping t, total 6H, J = 7Hz, CH_2CH_3); 2.60 (s, 3H, CH_3); 2.73 (s, 3H, CH_3); 4.33, 4.36 (2 overlapping q, total 4H, J = 7Hz, CH_2CH_3). ^{13}C NMR ($CDCl_3$, 67.8 MHz, δ): 13.89, 14.24, 14.33, 17.56 (2 CH_2CH_3, 2 CH_3); 60.97, 61.91 (2 CH_2CH_3); 109.56 (oxathiole *C*-4); 118.16 (thiazole *C*-5); 155.74 (oxathiole *C*-5); 157.86 (thiazole *C*-4); 160.75 (oxathiole CO_2Et); 162.51 (thiazole CO_2Et); 167.34, 168.51 (2 *C*-2).

Reaction of methyl 2-chloroacetoacetate with ammonium thiocyanate. Methyl 2-chloroacetoacetate (11.4g, 0.076 mol) in ethanol (25 mL) was added to a solution of ammonium thiocyanate (10.0 g, 0.130 mol) in water (25 mL) and stirred for 1.5h. The resultant precipitate was collected, washed with water (400 mL) and recrystallised from methanol giving **methyl 2-[2-amino-5-(methoxycarbonyl)-4-thiazolylthio]acetoacetate [7 (R = OMe; R' = H)]** as white needles (6.0 g, 52%), mp 161-162°. Found: C, 39.43; H, 3.93; N, 9.08%.

$C_{10}H_{12}N_2O_5S_2$ requires C, 39.46; H, 3.97; N, 9.21%. HRMS (m/z): 304.0186 (M^+); calcd 304.0188. MS (m/z, %): 304, *23* (M^+); 272, 46 (M^+-MeOH); 262, 13 (M^+-CH_2CO); 230, *46* (M^+-MeOH-CH_2CO); 43, *100* ($MeCO^+$). IR (ν_{max}): 3425, 3320,3210 (N-H st); 1735 (C=O st of chain CO_2Me); 1705 (C=O st of COMe); 1642 (C=O st of ring CO_2Me and enolised β-keto ester); 1615 (C=C st / N-H bend). UV (λ_{max} ,ε_{max}): 322, *1484* (thiazole ring); 266, *775* (keto-enol side-chain). ^1H NMR (DMSO-d_6, 250 MHz, δ):2.21, 2.39 (2 s, total 3H, enol $CH_3C(OH)$, keto CH_3CO); 3.69, 3.70, 3,73 (3 s, total 6H, CO_2CH_3 of enol chain, keto chain, ring); 5.64, 13.55 (2 s, total 1H, ex, keto C-*H*, enol O-*H*); 8.02, 8.11 (2 s, total 2H, ex, enol and keto NH_2). ^{13}C NMR (DMSO-d_6, 62.9 MHz, δ): 20.77 (enol $CH_3C(OH)$); 28.88 (keto CH_3CO); 51.24, 51.40, 52.49, 53.08 (4 OCH_3); 58.55 (keto *C*HS); 91.50 (enol *C*S); 100.69, 101.46 (2 *C*-5); 154.69, 158.59 (2 *C*-4); 161.51, 161.62 (2 ring CO_2Me); 166.72 (keto CO_2Me); 170.38, 170.54 (2 *C*-2); 172.50 (enol CO_2Me); 182.52 (enol $CH_3C(OH)$); 199.19 (keto CH_3CO).

Reaction of 3-chloro-2,4-pentanedione with potassium thiocyanate. ***A. In ethanol.*** 3-Chloro-2,4-pentanedione (6.7 g, 0.05 mol) in ethanol (30 mL) was added to a solution of potassium thiocyanate (5.5 g, 0.055 mol) in ethanol (200 mL) and stirred for 3h at 0°. On warming to room temperature the solvent was removed and the residue partitioned between ether (200 mL) and water (50 mL). The organic layer was dried (Na_2SO_4), filtered and evaporated to dryness giving an orange oil (7.0 g). Chromatographic separation on silica gel using $CHCl_3$ as eluant gave the following compounds *a* and *b* as the main products.

a. **3-(2-Amino-5-acetyl-4-thiazolylthio)pentane-2,4-dione [7 (R = Me; R' = H)].** White prisms (3.0 g, 44%), mp 208-212° (dec.) (EtOH) (lit[5] mp 200-228° (dec)). Found: C, 44.27; H, 4.48; N, 10.26; S, 22.95%. $C_{10}H_{12}N_2O_3S_2$ requires C, 44.11; H, 4.45; N, 10.30; S, 23.51%. HRMS (m/z): 272.0292 (M^+); calcd 272.0289. MS (m/z, %): 272, *20* (M^+); 230, *10* (M^+-CH_2CO); 212, *9* (M^+-CH_2CO-H_2O); 187, *35*; 43, *100* ($MeCO^+$). IR (ν_{max}): 3400, 3300, 3200 (N-H st); 1635sh (C=O st of COMe), 1620,1580 (C=O and C=C st of enolised β-diketone / N-H bend). UV (λ_{max} ,ε_{max}): 344, *1413* (thiazole ring); 272, *1536* (keto-enol side-chain). ^1H NMR (DMSO-d_6, 270 MHz, δ): 2.22 (s, 6H, 2 enol CH_3); 2.30 (s, 3H, ring $COCH_3$); 8.15 (s, 2H, ex, NH_2); 17.15 (s, 1H, ex, enol O*H*). ^{13}C NMR (DMSO-d_6, 67.8 MHz, δ): 24.42 (2 enol CH_3); 29.32 (ring $COCH_3$); 102.20 (*C*S); 114.44 (*C*-5); 157.05 (*C*-4); 170.52 (*C*-2); 186.31 (2 enol $CH_3C(OH)$); 196.63 (ring $COCH_3$).

b. **3-(2-Acetamido-5-acetyl-4-thiazolylthio)pentane-2,4-dione [7 (R = Me; R' = COMe)].** White prisms (2.8 g, 36%), mp 233-235° (EtOH). Found: C, 45.86; H, 4.49; N, 8.76; S, 19.97%. $C_{12}H_{14}N_2O_4S_2$ requires C, 45.85; H4.49; 8.91; S, 20.40%. HRMS (m/z): 314.0399 (M^+); calcd 314.0395. MS (m/z, %): 314, *15* (M^+); 272, *9* (M^+-CH_2CO); 254, *5* (M^+-CH_2CO-H_2O); 229, *18*; 187, 25; 43, *100* ($MeCO^+$). IR (ν_{max}): 3250, 3150 (N-H st); 1700,1540 (C=O st of NHCOMe); 1620 (C=O st of enolised β-diketone). UV (λ_{max} , ε_{max}): 334, *1089* (thiazole ring); 260, *2108* (keto-enol side-chain). ^1H NMR (DMSO-d_6, 270 MHz, δ): 2.22 (s, 3H, $NHCOCH_3$); 2.30 (s, 6H, 2 enol CH_3); 2.49 (s, 3H, ring $COCH_3$); 12.35 (s, 1H, ex, N*H*COMe); 17.21 (s, 1H, ex, enol O*H*). ^{13}C NMR (DMSO-d_6, 67.8 MHz, δ): 22.61 ($NHCOCH_3$); 24.51 (2 enol CH_3); 29.46 (ring $COCH_3$); 101.83 (*C*S); 119.80 (*C*-5); 155.04 (*C*-4); 160.56 (*C*-2); 169.57 (NH*C*OMe); 188.81 (2 enol $CH_3C(OH)$); 197.01 (ring *C*OMe).

B. In acetone. When the reaction was repeated in dry acetone under a N_2 atmosphere, **3-thiocyanato-2,4-pentanedione (4)** was obtained as an unstable solid (93%), mp 77-81° (lit[28] mp 78-81°). IR (ν_{max}): 2160 (SCN st); 1600 (C=O st of enolised β-diketone). ^1H NMR ($CDCl_3$, 80 MHz, δ): 2.50 (s, 6H, 2 enol CH_3); 17.10 (s, 1H, ex, enol O*H*).[11] When (4) was dissolved in ethanol containing potassium thiocyanate and subjected to the

reaction and isolation procedures described above, it gave the same mixture of products as before (TLC); the main compounds were again 7 (R = Me, R' = H) and 7 (R = Me, R' = COMe).

Desulphurisation of 7 (R = OEt; R' = H). Compound 7 (R = OEt; R' = H) (0.50 g, 0.015 mol) was dissolved in EtOH (50 mL) and Raney nickel (2.0 g, 20 equiv) was added. The mixture was heated under reflux for 16h, cooled, and filtered through a kieselguhr pad. After removal of solvent, the residue was chromatographed on silica gel (10 g), eluting with 5% MeOH/$CHCl_3$. This gave **ethyl 2-aminothiazole-5-carboxylate [8 (R = H)]** as white prisms (0.10 g, 39%), mp 160-162° (lit[29] mp 161-162°) (ether/light petroleum). Found: C, 42.04; H, 4.70; N, 15.66%. $C_6H_8N_2O_2S$ requires: C, 41.85; H, 4.68; N, 16.27%. HRMS (m/z): 172.0306 (M^+); calcd 172.0306. MS (m/z, %): 172, *72* (M^+); 144, 38 (M^+-C_2H_4); 127, *100* (M^+-OEt); 99, *32* (M^+- CO_2Et). UV (λ_{max} ,ε_{max}): 299, *1492*; 210, *473*. ^1H NMR (DMSO-d_6, 270 MHz, δ): 1.28 (t, 3H, J = 7Hz, OCH_2CH_3); 4.20 (q, 2H, J = 7Hz, OCH_2CH_3); 7.51 (s, 2H, ex, NH_2); 7.65 (s, 1H, ring *H*). ^{13}C NMR (DMSO-d_6, 67.8 MHz, δ): 13.98 (OCH_2CH_3); 59.70 (OCH_2CH_3); 114.90 (*C*-5); 147.15 (*C*-4); 161.28 (CO_2Et); 173.34 (*C*-2).

Decarbethoxylation[30] of 7 (R = OEt; R' = H). Compound 7 (R = OEt; R' = H) (0.50 g, 0.0015 mol) was dissolved in DMSO (5 mL) containing water (0.05 mL). Sodium chloride (0.15 g, 0.0025 mol) was added and the mixture heated at 150° for 5h. Water (30 mL) was added to the cooled solution and the resulting solid recrystallised from EtOH/H_2O giving **ethyl 2-amino-4-(1-propanoylthio)thiazole-5-carboxylate [8 (R = SCH_2COMe)]** as white prisms (0.19 g, 47%) mp 129-130°. Found: C, 41.73; H, 4.57; N,10.38%. $C_9H_{12}N_2O_3S_2$ requires: C, 41.52; H,4.65; N, 10.76%. HRMS (m/z): 260.0287 (M^+); calcd 260.0289. MS (m/z, %); 260, *44* (M^+); 217, *100* (M^+-MeCO); 189, *20* (M^+-MeCO-C_2H_4); 171, *32* (M^+-$MeCOCH_2S$); 159, *82*; 43, *44* ($MeCO^+$). IR (ν_{max}): 3420, 3350, 3300, 3200 (N–H st); 1720, 1705 (C=O st of CO_2Et); 1655 (C=O st of MeCO); 1625, 1615 (N-H bend). UV (λ_{max} ,ε_{max}): 321, *1463*; 247, *1107*. ^1H NMR ($CDCl_3$, 270 MHz, δ): 1.31 (t, 3H, J = 7Hz, OCH_2CH_3); 2.30 (s, 3H, $COCH_3$); 3.89 (s, 2H, SCH_2); 4.27 (q, 2H, J = 7Hz, OCH_2CH_3); 5.30 (s, 2H, ex, NH_2). ^{13}C NMR (DMSO-d_6, 67.8 MHz, δ): 14.41 (OCH_2CH_3); 29.14 ($COCH_3$); 41.66 (SCH_2); 59.86 (OCH_2CH_3); 101.45 (*C*-5); 157.12 (*C*-4); 161.27 (CO_2Et); 170.26 (*C*-2); 202.96(*C*OMe).

Acetylation of 7 (R = OEt; R' = H). Compound 7 (R = OEt; R' = H) (0.50 g, 0.0015 mol) was dissolved in acetic anhydride (10 mL) containing conc sulphuric acid (3 drops). The solution was heated under reflux for 10 min, cooled, and added to water (100 mL). The product was filtered off, washed with water, and recrystallised from aqueous ethanol to give **compound 9** as yellow prisms (0.26 g, 48%), mp 132-134°. Found: C, 47.11; H, 4.45; N, 7.85%. $C_{14}H_{16}N_2O_5S_2$ requires: C, 47.18; H, 4.52; N, 7.86%. MS (m/z, %): 356, *46* (M^+); 314, *34* (M^+-CH_2CO); 269, *5* (M^+-CH_2CO-OEt); 241, *42* (M^+-CH_2CO-CO_2Et); 43,*100* ($MeCO^+$). IR (ν_{max}): 1710 (C=O st of CO_2Et); 1680 (C=N st); 1620 (C=O st of NCOMe). UV (λ_{max},ε_{max}): 382, *2670*; 330, *2225*; 280, *534*; 233, *3702*. ^1H NMR ($CDCl_3$, 250 MHz, δ): 1.37, 1.41 (2 overlapping t, total 6H, J = 7Hz, 2 OCH_2CH_3); 2.36 (s, 3H, ring CH_3); 3.25 (s, 3H, $COCH_3$); 4.35, 4.40 (2 overlapping q, total 4H, J = 7Hz, 2 OCH_2CH_3). ^{13}C NMR ($CDCl_3$, 62.9 MHz, δ): 14.16, 14.42 (2 OCH_2CH_3); 15.39 (ring CH_3); 27.13 ($NCOCH_3$); 61.57, 62.27 (2 OCH_2CH_3); 97.57, 118.03, 142.45, 143.49, 164.00 (5 ring *C*); 161.14, 161.63 (2 CO_2Et); 180.61 (NCOMe). In the absence of acid , the reaction was slower and gave predominantly 7 (R = OEt; R' = COMe).

Hydrolysis of 14. The oxathiole **14** (0.50 g, 0.0022 mol) was dissolved in ethanol (3 mL) and added to 1M HCl (20 mL). The mixture was heated on a steam bath for 1h and then cooled. The resulting precipitate was collected, washed with water, and recrystallised from aqueous ethanol to give **ethyl 4-methylthiazolin-2-one-5--carboxylate (20)** as white prisms (0.19 g, 41%), mp 175-177° (lit.[5] mp 175°). Found: C, 44.93; H, 4.92; N, 7.52%. $C_7H_9NO_3S$ requires: C, 44.91; H, 4.85; N, 7.48%. HRMS (m/z): 187.0306 (M^+); calcd 187.0303. MS (m/z, %): 187, *100* (M^+); 159, *40* (M^+-C_2H_4 or CO); 142, *47* (M^+-OEt); 113, *57*; 42, *82*. IR (ν_{max}): 3150 (N-

H st); 1705, 1640, 1600 (C=O and C=C st). UV (λ_{max}, ε_{max}): 278, *1092*. ^{1}H NMR ($CDCl_3$, 270 MHz, δ): 1.33 (t, 3H, J = 7Hz, OCH_2CH_3); 2.50 (s, 3H, ring CH_3); 4.27 (q, 2H, J = 7Hz, OCH_2CH_3); 10.80 (s, 1H, ex, N*H*). ^{13}C NMR ($CDCl_3$, 67.8 MHz, δ): 13.75 (OCH_2CH_3); 14.30 (ring CH_3); 61.24 (OCH_2CH_3); 105.08 (*C*-5); 141.91 (*C*-4); 161.58 (CO_2Et); 174.08 (*C*-2). This compound was also prepared in 41% yield by the reaction of ethyl 2-chloroacetoacetate with ammonium thiocarbamate.[5]

Acetylation of 20. The thiazolin-2-one **20** (0.50 g, 0.0027 mol) was dissolved in dry dichloromethane (20 mL) and cooled to 0°. Triethylamine (0.29 g, 0.0028 mol) was added, followed by acetyl chloride (0.22 g, 0.0028 mol). After being stirred at 0° for 4h, the solution was washed with 5% aqueous $NaHCO_3$ solution and dried (Na_2SO_4). Removal of solvent yielded pure **ethyl 2-acetoxy-4-methylthiazole-5-carboxylate (21)** as white prisms (0.41 g, 67%), mp 57-59°. Found: C, 47.28; H, 4.87; N, 5.76; S, 13.91%. $C_9H_{11}NO_4S$ requires: C, 47.16; H, 4.84; N, 6.11; S, 13.99%. HRMS (m/z): 229.0390 (M^+); calc 229.0409. MS (m/z, %): 229, *7* (M^+); 187, *95* (M^+-CH_2CO); 159, *27* (M^+-CH_2CO-C_2H_4 or CO); 142, *26*; 113, *30*; 43, *100* ($MeCO^+$). IR (ν_{max}): 1755, 1720 (C=O st). UV (λ_{max}, ε_{max}): 267, *762*; 202, *984*. ^{1}H NMR ($CDCl_3$, 270 MHz, δ): 1.34 (t, 3H, J = 7Hz, OCH_2CH_3); 2.67 (s, 6H, superimposed ring CH_3 and $OCOCH_3$); 4.29(q, 2H, J = 7Hz, OCH_2CH_3). ^{13}C NMR ($CDCl_3$,. 67.8 MHz, δ): 14.21 (OCH_2CH_3); 15.21 (ring CH_3); 27.34 ($COCH_3$); 61.72 (OCH_2CH_3); 106.27 (*C*-5); 142.47 (*C*-4); 161.15 (CO_2Et); 170.66 (*C*OMe); 171.21 (*C*-2).

Diethyl thiocyanatomalonate (5).[31] Diethyl chloromalonate (6.6 g, 0.034 mol) was added to a solution of potassium thiocyanate (7.7 g, 0.079 mol) in ethanol (50 mL) and the mixture heated under reflux with stirring for 1 h. The cooled mixture was poured in to water (200 mL) and extracted with diethyl ether (3 x 50 mL). The combined organic layers were dried ($CaCl_2$), filtered and evaporated under reduced pressure to yield pure **5** (TLC) as a pale yellow liquid (6.9 g, 93%). Found: C, 44.01; H, 5.19; N, 6.35%. $C_8H_{11}NO_4S$ requires C, 44.23; H, 5.10; N, 6.45%. IR (film): 2165 (SCN st); 1730 (C=O st) cm^{-1}. ^{1}H NMR ($CDCl_3$, 80 MHz): δ 1.32 (6H, t, *J* = 7 Hz, CH_3); 4.32 (4H, q, *J* = 7 Hz, CH_2); 4.68 (1H, s, C*H*). MS (m/z, %): 217, *2* (M^+); 190, *19* (M^+ - HCN); 117, *25* (M^+ - HCN - COOEt); 45, *100*.

Ethyl 2-methyl-2-thiocyanatoacetoacetate (6). Treatment of ethyl 2-methylacetoacetate with sulphuryl chloride[32] gave ethyl 2-chloro-2-methylacetoacetate as a pale yellow oil (94%) which was used immediately to minimise decomposition due to elimination of HCl. This chloride (2.0 g, 0.011 mol) was added to a solution of ammonium thiocyanate (1.7 g, 0.022 mol) in ethanol (20 mL) and, after 7 days at rt, the resulting mixture was poured into water (100 mL) and extracted with diethyl ether (2 x 50 mL). The combined organic layers were dried ($CaCl_2$), filtered and evaporated under reduced pressure to yield a red oil (2.1 g) from which pure **6** (TLC) was isolated as a pale yellow oil (1.4 g, 62%) by chromatography on silica gel. Found: C, 47.95; H, 5.80; N, 6.71%. $C_8H_{11}NO_3S$ requires C, 47.75; H, 5.51; N, 6.96%. IR (film): 2165 (SCN st); 1720 (C=O st) cm^{-1}. MS (m/z, %): 201, *8* (M^+); 186, *17* (M^+ - CH_3); 159, *16* (M^+ - CH_2CO); 142, *14* (M^+ - HSCN); 59, *50* ($HSCN^+$); 43, *100* ($MeCO^+$).

The following **model compounds** were prepared to assist the assignments described above. Some have been described before in the literature but without the spectroscopic data required in this investigation.

Methyl 2-amino-4-methylthiazole-5-carboxylate. Using the general method described by Barton *et al*,[33] this compound was prepared on a 0.033 mol scale from methyl 2-chloroacetoacetate and thiourea as white needles (3.0 g, 53%), mp 231.5-233° (EtOH). Found: C, 41.83; H, 4.63; N, 16.16%. $C_6H_8N_2O_2S$ requires C, 41.84; H, 4.68; N, 16.26%. MS (m/z, %): 172, *92* (M^+); 141,*100* (M^+-OMe); 113, *25* (M^+-OMe-CO); 71, *22*; 45, *33*. IR (ν_{max}): 3360, 3280 (N-H st); 1665 (C=O st); 1635 (N-H bend). UV (λ_{max}, ε_{max}): 300, *1552*. ^{1}H NMR

($CDCl_3$, 80 MHz, δ): 2.55 (s, 3H, ring CH_3); 3.80 (s, 3H, OCH_3); 5.19 (s, 2H, ex, NH_2). ^{13}C NMR (DMSO-d_6, 20 MHz, δ): 16.95 (ring CH_3); 51.04 (OCH_3); 107.07 (*C*-5); 159.49 (*C*-4); 162.32 (CO_2Me); 170.31 (*C*-2).

Ethyl 2-amino-4-methylthiazole-5-carboxylate [8 (R = Me)]. This compound was prepared as above[33] on a 0.054 mol scale from ethyl 2-chloroacetoacetate and thiourea as white prisms (7.0 g, 69%), mp 178-179° (EtOH) (lit[34] mp 176°). MS (m/z, %): 186, *90* (M^+); 158, *24*(M^+-C_2H_4); 141, *100* (M^+-OEt); 114, *48* (M^+-OEt-HCN); 71, *33*; 45, *40*. IR (ν_{max}): 3380, 3310 (N-H st); 1670 (C=O st); 1645 (N-H bend). UV (λ_{max}, ε_{max}): 298, *1606*. ^1H NMR ($CDCl_3$, 80 MHz, δ): 1.33 (t, 3H, J = 6.5Hz, OCH_2CH_3); 2.53 (s,3H, ring CH_3); 4.27 (q, 2H, J = 6.5Hz, OCH_2CH_3); 5.43 (s,2H, ex, NH_2). ^{13}C NMR (DMSO-d_6, 20 MHz, δ): 14.20 (OCH_2CH_3); 16.99 (ring CH_3); 59.65 (OCH_2CH_3); 107.63 (*C*-5); 159.24 (*C*-4); 161.96 (CO_2Et); 170.29 (*C*-2).

Ethyl 2-acetamido-4-methylthiazole-5-carboxylate. This compound was prepared on a 5.4 mmol scale, by heating **8** in acetic anhydride under reflux for 1.5h, as white prisms (1.0 g, 81%), mp 227-228° (MeOH/H_2O). Found: C, 47.25; H, 5.46; N, 12.18%. $C_9H_{12}N_2O_3S$ requires C, 47.36; H, 5.30; N, 12.28%. MS (m/z, %): 228, *18* (M^+); 185, *100* (M^+-MeCO); 158, 19 (M^+-MeCO-HCN); 141, *36*; 114, *26*; 43, *56* ($MeCO^+$). IR (ν_{max}): 3170 (N-H st); 1710 (ester C=O st); 1665 (amide C=O st / N-H bend). UV (λ_{max},ε_{max}): 291, *1533*. ^1H NMR ($CDCl_3$, 80 MHz, δ): 1.36 (t, 3H, J = 7Hz, OCH_2CH_3); 2.26 (s, 3H, ring CH_3); 2.64 (s, 3H, $NHCOCH_3$); 4.32 (q, 2H, J = 7Hz, OCH_2CH_3); 10.48 (s, 1H, ex, NH). (δNH is 12.40 in DMSO-d_6). ^{13}C NMR (DMSO-d_6, 20 MHz, δ): 14.02 (OCH_2CH_3); 16.79 (ring CH_3); 22.31 ($NHCOCH_3$); 60.22 (OCH_2CH_3); 113.85 (*C*-5); 155.89 (*C*-4);159.52 (*C*-2); 162.04 (CO_2Et); 168.97 ($NHCOCH_3$).

Ethyl 2-methoxy-4-methylthiazole-5-carboxylate (17).[24b] Ethyl 4-methylthiazolin-2-one-5-carboxylate (20) (1.0 g, 5.3 mmol) was dissolved in dry dichloromethane (30 mL). Trimethyloxonium tetrafluoroborate (1.05 g, 7.1 mmol) was added and the mixture stirred for 26h. The resulting solution was washed with 5% aqueous sodium bicarbonate (3 x 25 mL), dried (Na_2SO_4), and evaporated to dryness. The residue was chromatographed on silica gel (10 g). Elution with dichloromethane gave a colourless oil which crystallised from pentane (10 mL at -20° giving **17** as white prisms (0.5 g, 47%), mp 36-38°. Found: C, 47.65; H, 5.43; N, 6.77%. $C_8H_{11}NO_3S$ requires C, 47.75; H, 5.51; N, 6.96%. HRMS (m/z): 201.0461 (M^+); calcd 201.0460. MS (m/z, %): 201, *32* (M^+); 172, *13* (M^+- Et); 156, *31* (M^+- OEt); 129, *11* (M^+-OEt-HCN); 113,*15*; 56, *32*; 28,*100*. IR (ν_{max}): 1715 (C=O st). UV (λ_{max}, ε_{max}): 269, *1209*; 202, *568*. ^1H NMR ($CDCl_3$, 270 MHz, δ): 1.34 (t, 3H, J = 7Hz, OCH_2CH_3); 2.60 (s, 3H, ring CH_3); 4.07 (s, 3H, OCH_3); 4.28 (q, 2H, J = 7Hz, OCH_2CH_3). ^{13}C NMR ($CDCl_3$ 67.8 MHz, δ): 14.33 (OCH_2CH_3); 17.45 (ring CH_3); 58.50 (OCH_3); 60.83 (OCH_2CH_3); 114.31 (*C*-5); 156.68 (*C*-4); 162.36 (CO_2Et); 175.81 (*C*-2).

Ethyl N,4-dimethylthiazolin-2-one-5-carboxylate (18).[24a] Ethyl 4-methylthiazolin-2-one-5-carboxylate (20) (1.0 g, 5.3 mmol) was dissolved in ethanol (30 mL) and potassium t-butoxide (0.6 g, 5.4 mmol) was added. Methyl iodide (1.1 mL, 17 mmol) was added and the solution was heated to 60° for 2h. After removal of solvent *in vacuo*, the residue was dissolved in dichloromethane, washed with 5% aqueous sodium bicarbonate solution (3 x 25 mL), dried (Na_2SO_4), and the solvent removed. The product was chromatographed on silica gel (10 g). Elution with dichloromethane gave a solid which crystallised from ethyl acetate / light petroleum as white prisms (0.64 g, 60%), mp 63-64°. Found: C, 47.59; H, 5.50; N, 6.93%. $C_8H_{11}NO_3S$ requires C, 47.75; H, 5.51; N, 6.96%. HRMS (m/z): 201.0461 (M^+); calcd 201.0460. MS (m/z,%): 201,*47* (M^+); 173, *19* (M^+-C_2H_4); 156, *23* (M^+-OEt); 56,*100*. IR (ν_{max}): 1680, 1660 (C=O st). UV (λ_{max}, ε_{max}): 280, *1206*; 204, *630*. ^1H NMR (DMSO-d_6, 270 MHz, δ): 1.24 (t, 3H, J = 7Hz, OCH_2CH_3); 2.55 (s, 3H, ring CH_3); 3.25 (s, 3H, NCH_3); 4.20 (q, 2H, J = 7Hz, OCH_2CH_3). ^{13}C NMR (DMSO-d_6, 67.8 MHz, δ): 13.10 (ring CH_3); 14.10 (OCH_2CH_3); 29.56 (NCH_3); 60.72(OCH_2CH_3); 100.12 (*C*-5); 145.77 (*C*-4); 161.04 (CO_2Et); 169.32 (*C*-2).

Keto-Enol Studies. These were carried out at 80 MHz using 10^{-1}M solutions. Keto-enol contents were determined (±1%) from the integrated areas of the CH_3CO and $CH_3C(OH)$ signals. Equilibrium was established within 0.5h as shown by measurements made over a 48h period. Thermodynamic parameters were derived in the usual way;[13] for the plot of $\ln K$ *v* $1/T$, the correlation coefficient was 0.9999. The data are collected in Table 1.

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