Reaction of 2-Aminothiazoles with Reagents containing a C–Halogen and a C=O Electrophilic Centre

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Seven reagents of different types having in common a C–Hal and a C=O electrophilic centre have been used in a study of their reactions with 2-aminothiazoles. Three reagents, $CHBrAc_2$ and $ROCHBrCO_2Et$ (R = Me, Ph), gave imidazo[2,1-*b*]thiazoles, thus providing useful routes to the 5-acetyl and 5-ethoxycarbonyl derivatives. Unexpectedly, the solvent (acetone) was involved in the reaction of the fourth reagent, $CHBr(CO_2Et)_2$, with 2-aminothiazole which led to 5,5-di(ethoxycarbonyl)-6,6-dimethyl-5,6-dihydroimidazo[2,1-*b*]thiazole (yield 81%). With the last three reagents ($AcCHBrNO_2$, BzCHBrCN and $ICH_2CO_2C_6H_4NO_2$-*p*) the outcome was simpler, *viz.*, the formation of 2-amidothiazoles.

It is proposed that electrophilic attack by the *endo*-N of the 2-aminothiazole is the first step in all cases. This occurs at the C–Hal centre of the first four reagents and is followed by cyclisation to the *exo*-N. In the last three electrophiles the presence of groups well suited to leaving as stabilised anions favours addition to the C=O group; the intermediates so formed subsequently isomerise to the more stable *exo*-N substituted products.

Simple α-bromo ketones react at the *endo*-N of 2-aminothiazoles; bromide is displaced and subsequent cyclisation between the carbonyl and amino groups gives imidazo[2,1-*b*]thiazoles.[1,2] During their extensive investigations of the parent 2-aminothiazole Robert and co-workers[3] examined its reactions with the more complex electrophiles AcCHBrCOR (R = Me, Ph, OEt), and found that the outcome varied with the nature of the electrophile and the solvent used. With 2-bromoacetylacetone in acetone at 20 °C displacement of bromide gave 3-(2,4-dioxopentan-3-yl)-2,3-dihydrothiazol-2-ylideneammonium bromide, but with 2-bromobenzoylacetone this process was accompanied by an acetyl migration which led to 3-benzoylmethyl-2-acetylimino-2,3-dihydrothiazolium bromide.[3b] In boiling ethanol the bromo diketones afforded the salts of 5-acetyl- and 5-benzoyl-6-methylimidazo[2,1-*b*]thiazole in good yield, and the 5-acetyl compound was also formed under these conditions from the 2,4-dioxopentan-3-yl salt. The bromo ester $AcCHBrCO_2Et$ was much less reactive; prolonged boiling in ethanol was required to form 5-ethoxycarbonyl-6-methylimidazo[2,1-*b*]thiazole (yield 20%).[3a] 2-Aminothiazole and 2-amino-4-methylthiazole have been condensed[4] with the homologous ester $AcCHBrCH_2CO_2Et$ which, having a more remote carboxylate group, might have been expected to react in a manner akin to that of a simple bromo ketone. Complex mixtures were formed, however, and no product was isolated in a yield greater than 10%. It is surprising, for reasons discussed later, that the main product from 2-amino-4-methylthiazole involves substitution at the *endo*-N centre.

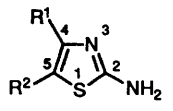
The present development of the topic is concerned with the reactions between 2-aminothiazoles and reagents of different types having in common a C–Hal and a C=O electrophilic centre. There are four possibilities for the first step, *viz.*, attack by the *endo*- or the *exo*-N at either centre, and a variety of systems could be formed. Scheme 1 shows the pairs of reactants studied and the results obtained. (One solvent, acetone, was used throughout in order to simplify the interpretation.)

2-Amino-5-methylthiazole **1B** reacts with 3-bromopentane-2,4-dione **2** in the manner established for the parent 2-aminothiazole **1a** by Robert *et al.*[3] The salts **8a**,[3b] **8b** formed by *endo*-N displacement of bromine at room temperature are readily cyclised by heating, and this leads conveniently to the 5-acetylimidazo[2,1-*b*]thiazoles **9A**,[3a] **9B**. The ester prepared[3a] from 2-aminothiazole **1A** and ethyl 2-bromo-3-oxobutanoate **3a** in boiling ethanol was obtained more efficiently using acetone as solvent and a modified work-up. Similar esters were prepared using the bromo ester **3a** with 2-amino-5-methylthiazole **1B**, and the 2-bromo-3-phenyl ester **3b** with the aminothiazoles **1A**, **1C** and **1D**. Although there seemed little doubt that the first product had been correctly formulated as the 5-ethoxycarbonyl-6-methylimidazothiazole **10Aa** it seemed prudent, in view of the later work,[4] to exclude the possible isomeric 6-ethoxycarbonyl-5-methyl (or phenyl) structures for compounds **10**. Distinction between the alternatives could not be made from the spectrometric data; identification of the imidazothiazoles formed by removing the ethoxycarbonyl groups was required. The esters were resistant to attempted hydrolysis under the standard acidic conditions, presumably because *O*-protonation leads to the stable ions **15**. However, the carboxylic acids obtained by alkaline hydrolysis were really decarboxylated by heating with hydrochloric acid, presumably *via* the intermediates **16** formed by protonation at C-5. Of the four esters treated in this way three gave known[2] 6-methyl- and 6-phenylimidazothiazoles **13Aa**, **Ab**, **Cb**, and the product from the fourth **10Db** was shown to be 2-benzyl-6-phenylimidazo[2,1-*b*]thiazole **13Db** by an unequivocal synthesis based on 2-amino-5-benzylthiazole **1D**.

The reaction between 2-aminothiazole and diethyl bromomalonate **4** took a different course and gave a product (yield 81%) shown by spectrometric examination to have structure **11**. Acetone is involved in the reaction, a feature unique to diethyl bromomalonate of the electrophiles studied here. Ring closure of the intermediates **17** to the imidazothiazole-5-carboxylates **10** involves nucleophilic attack on a ketone group. Such a process will be less favourable in the corresponding intermediate **18** from diethyl bromomalonate (where only a less electrophilic ester group is available) and imine formation with an external ketonic component (acetone) is preferred. Completion of the sequence probably involves removal of the acidic proton by a further molecule of 2-aminothiazole to give an ylide **19** which is favourably constituted for generation of the product **11** by an electrocyclic process. Product **11** was converted into a mono-ester **14** as shown in Scheme 2.

A simple outcome, formation of 2-amidothiazoles **12**, was observed with the other three electrophiles **5**, **6** and **7**. These

2-Aminothiazoles



1

Electrophiles

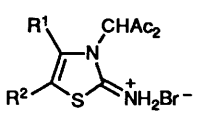
$CHBrAc_2$ $R^3COCHBrCO_2Et$ $CHBr(CO_2Et)_2$

2 3 4

$AcCHBrNO_2$ $BzCHBrCN$ $ICH_2CO_2C_6H_4NO_2$-*p*

5 6 7

Products



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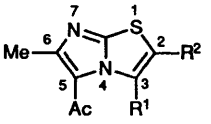

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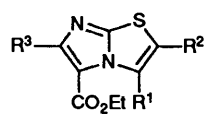

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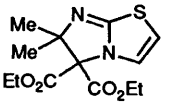
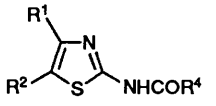


11



12

A, $R^1 = R^2 = H$; **B**, $R^1 = H$, $R^2 = Me$; **C**, $R^1 = Me$, $R^2 = H$; **D**, $R^1 = H$, $R^2 = PhCH_2$; **a**, $R^3 = Me$; **b**, $R^3 = Ph$; **c**, $R^4 = Me$; **d**, $R^4 = Ph$; **e**, $R^4 = CH_2I$

Reactions: Me_2CO was used as solvent at the temperature (°C) shown; reactions occurring at 56 °C proceeded only very slowly at 20 °C. The products, apart from **8A** and **8B**, were obtained after basification. Yields are shown in parentheses.

1A + **2** $\xrightarrow[(71\%)]{20\ °C}$ **8A**[a] $\xrightarrow[(79\%)]{56\ °C}$ **9A**[b]

1B + **2** $\xrightarrow[(74\%)]{20\ °C}$ **8B** $\xrightarrow[(78\%)]{56\ °C}$ **9B**

1A + **3a** $\xrightarrow[(62\%)]{56\ °C}$ **10Aa**[b] **1A** + **5** $\xrightarrow[(69\%)]{20\ °C}$ **12Ac**[c]

1B + **3a** $\xrightarrow[(63\%)]{56\ °C}$ **10Ba** **1B** + **5** $\xrightarrow[(71\%)]{20\ °C}$ **12Bc**[d]

1A + **3b** $\xrightarrow[(64\%)]{56\ °C}$ **10Ab** **1A** + **6** $\xrightarrow[(68\%)]{56\ °C}$ **12Ad**[e]

1C + **3b** $\xrightarrow[(64\%)]{56\ °C}$ **10Cb** **1D** + **6** $\xrightarrow[(60\%)]{56\ °C}$ **12Dd**[f]

1D + **3b** $\xrightarrow[(61\%)]{56\ °C}$ **10Db** **1A** + **7** $\xrightarrow[(57\%)]{20\ °C}$ **12Ae**[g]

1A + **4** $\xrightarrow[(81\%)]{20\ °C}$ **11**

[a] Ref. 3*b*. [b] Ref. 3*a*. [c] Ref. 11. [d] Ref. 12. [e] Ref. 13. [f] Ref. 14. [g] Not fully purified.

Scheme 1 Reactions of 2-aminothiazoles with electrophiles

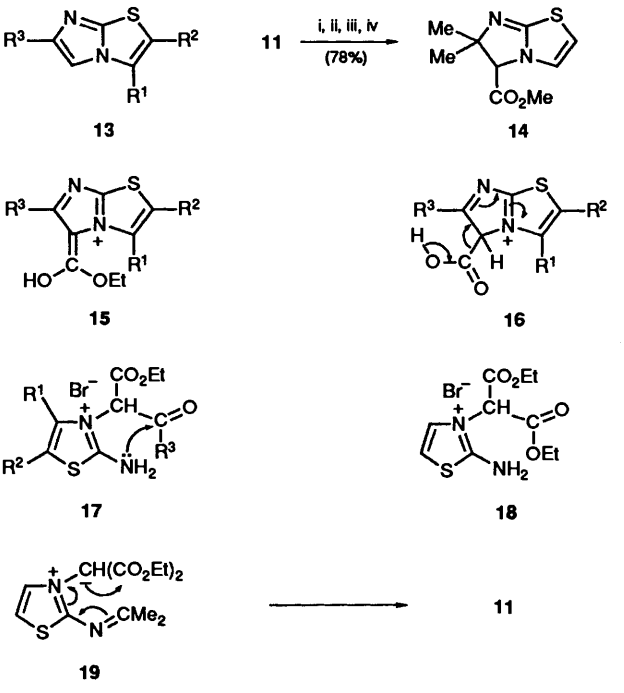
reagents thus differ from those discussed previously in two respects: nucleophilic attack by the 2-aminothiazole occurs at the C=O group rather than at the halogen-bearing carbon, and, in the products, there are now new bonds to the *endo*-N atoms. With all the electrophiles the first step will involve competition between reversible addition to a C=O group and irreversible displacement of halogen, the reactions shown in Scheme 3. If the addition is followed rapidly by departure of a leaving group this pathway will supervene. Such applies with electrophiles **5**, **6** and **7** which have groups well suited for leaving as stabilised anions ($^-CHBrNO_2$, ^-CHBrCN, $^-OC_6H_4NO_2$-*p*). The second difference could be interpreted as indicating direct attack by these electrophiles at the *exo*-N centres of the 2-aminothiazoles. However, there is evidence[5] that *endo*-N attack is the preferred mode irrespective of the electrophile's nature, and that *exo*-N substituted products arise from subsequent isomerisation. An explanation is suggested in Scheme 4. The transition state leading to the *endo*-N isomer is stabilised by delocalisation of the developing positive charge over the two N atoms, but the

10Aa $\xrightarrow[(82\%)]{i,\ ii}$ **13Aa**[a]

10Ab $\xrightarrow[(85\%)]{i,\ ii}$ **13Ab**[a]

10Cb $\xrightarrow[(84\%)]{i,\ ii}$ **13Cb**[a]

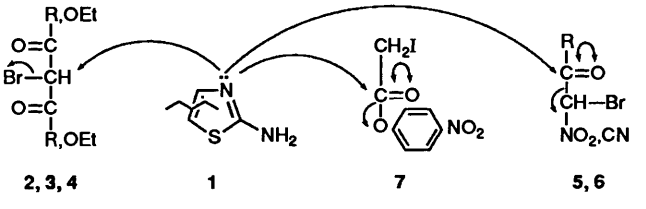
10Db $\xrightarrow[(79\%)]{i,\ ii}$ **13Db** $\xleftarrow[(76\%)]{v}$ **1D**



Reagents: i, KOH–EtOH, heat; ii, HCl–H_2O, heat; iii, evaporate to dryness; iv, H_2SO_4–MeOH, heat; v, B_2CH_2Br used in general synthesis.[a]

[a] Ref. 2.

Scheme 2 Reactions of products, and formation of product **11**

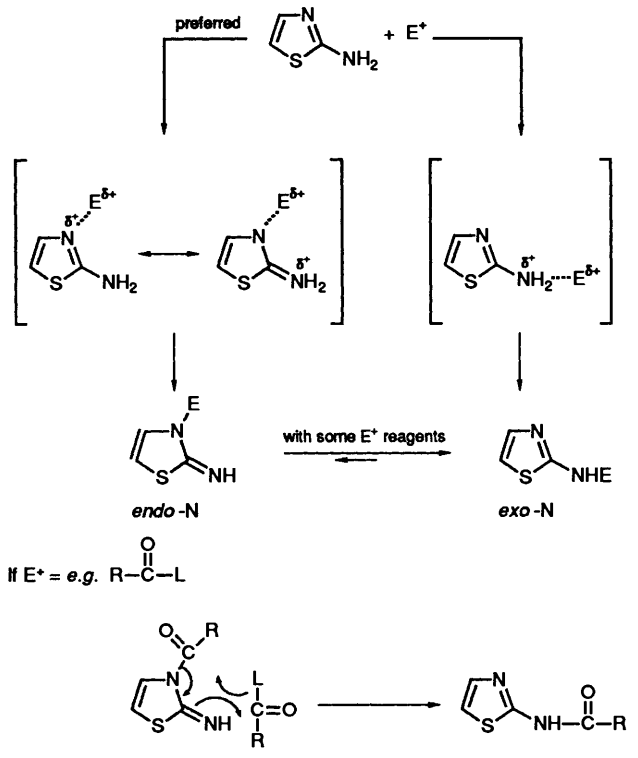


Scheme 3 Reactions at different sites of electrophiles

product is less stable than the *exo*-N isomer which has the aromatic thiazole system. Isomerisation occurs if the process has a sufficiently low activation energy: that shown for an amide involves a second molecule of the electrophile in a 6-membered transition state, and is thought to apply to the formation of products **12**.

Experimental

General directions are given in ref. 6. ^1H NMR spectra were obtained using solutions of the salts in $(CD_3)_2SO$, and of the other compounds in $CDCl_3$. Column chromatography was carried out on silica gel (60–120 mesh). Light petroleum refers to the fraction boiling in the range 85–95 °C. The 2-aminothiazoles are known: **1A–C**,[7] **1D**.[2] The reagents **2**, **3a**, **3b**, **5** and **6** were obtained by brominating CH_2Ac_2, $RCOCH_2CO_2Et$



Scheme 4 Formation of *endo*- and *exo*-N substituted products

(R = Me, Ph), the product from MeCN and Na,[8a] and $BzCH_2CN$, respectively, using the method (Br_2 in CCl_4–H_2O at 0 °C) described previously,[8b] and the purity of the reagents (>94%) was established by ^1H NMR examination. The published constants of reagents **4**[9] and **7**[10] were confirmed.

$BzCH_2CN$ was prepared safely as follows. Finely powdered $BzCH_2Br$ (10 g) was added to a stirred solution of KCN (10 g) in water (30 cm^3)–EtOH (30 cm^3) contained in a 2-neck flask. A stream of air was drawn through the solution and then through a scrubber containing aqueous sodium hypochlorite. The mixture was heated at 50 °C for 1 h, cooled, diluted with water and washed with CH_2Cl_2. The solution was returned to the aspirated apparatus and aq. HCl (10 mol dm^{-3}; 20 cm^3) was added. After 20 min the precipitate was collected, and crystallised (MeOH) to give $BzCH_2CN$ (6.96 g), m.p. 81–82 °C (lit.,[11] 80–81 °C).

Three procedures (A, B and Basification) used in many experiments are described fully only in the following section.

The Salts **8** *and Imidazothiazoles* **9**.—*Procedure A.* A filtered solution of the bromo diketone **2** (6.95 g) in dry Me_2CO (30 cm^3) was added during 10 min to a stirred (previously filtered) solution of 2-aminothiazole **1A** (3.81 g) in dry Me_2CO (30 cm^3) at 20 °C. After 24 h the precipitate was collected, and washed with CCl_4 to give the salt **8A** (7.55 g), m.p. 222–225 °C (lit.,[3b] 230–232 °C).

Procedure B. A solution of the salt (5.25 g) in Me_2CO (60 cm^3) was boiled under reflux for 4 h, and the solvent was evaporated at 60 °C, 15 mmHg.

Basification. The residue was stirred vigorously for 15 min at 20 °C with aq. $NaHCO_3$ (2 mol dm^{-3}; 50 cm^3)–CH_2Cl_2 (50 cm^3). Extraction of the aqueous layer with more CH_2Cl_2, work-up of the combined CH_2Cl_2 solutions, and evaporation of solvent at 20 °C, 15 mmHg, gave 5-acetyl-6-methylimidazo[2,1-*b*]thiazole **9A** (2.88 mg), m.p. 131–133 °C (from CH_2Cl_2–light petroleum) (lit.,[3a] 132–134 °C).

Similarly, the bromo diketone **2** and 2-amino-5-methylthiazole **1B** gave *2-amino-5-methyl-3-(2,4-dioxopentan-3-yl)-2,3-dihydrothiazol-2-ylideneammonium bromide* **8B** (74%), m.p. 240–243 °C (Found: C, 36.7; H, 4.6; N, 9.5. $C_9H_{13}BrN_2O_2S$ requires C, 36.9; H, 4.5; N, 9.6%); δ_H 2.01 (s) and 2.15 (s) (together 6 H, two Me of keto and enol forms respectively), 2.20 (3 H, s, 5-Me), 6.70 (0.8 H, s, CH of keto form) and 6.93 (1 H, s, 4-H). Cyclisation followed by basification gave *5-acetyl-2,6-dimethylimidazo*[2,1-b]*thiazole* **9B** (78%), m.p. 78–80 °C (water) (Found: C, 55.8; H, 5.25; N, 14.4. $C_9H_{10}N_2OS$ requires C, 55.6; H, 5.2; N, 14.4%); δ_H 2.48 (3 H, s, 2-Me), 2.50 (3 H, s, 6-Me), 2.67 (3 H, s, MeCO) and 8.10 (1 H, s, 3-H); *m/z* 194 (M^+, 85%) and 179 ($M - Me^+$, 100); ν_{max}/cm^{-1} 1632.

The Esters **10**.—A solution of the bromo ester **3a** (7.29 g) and 2-aminothiazole **1A** (3.28 g) in Me_2CO (60 cm^3) was used in procedure B. Basification gave material which was chromatographed on silica gel (60–120 mesh; 250 g). Et_2O–light petroleum (b.p. 60–80 °C) (3:7) eluted ethyl 6-methylimidazo-[2,1-*b*]thiazole-5-carboxylate **10Aa** (4.27 g), b.p. 120–122 °C, 0.03 mmHg, m.p. 104–105 °C (lit.,[3a] 108 °C); ^1H NMR signals as reported;[3a] ν_{max}/cm^{-1} 1688.

Similarly, the reagent **3a** and 2-amino-5-methylthiazole **1B** gave *ethyl 2,6-dimethylimidazo*[2,1-b]*thiazole-5-carboxylate* **10Ba** (63%), m.p. 78–79 °C (CH_2Cl_2–light petroleum) (Found: C, 53.5; H, 5.3; N, 12.4. $C_{10}H_{12}N_2O_2S$ requires C, 53.55; H, 5.4; N, 12.5%); δ_H 1.40 (3 H, t, *J* 8, CH_2CH_3), 2.40 (3 H, s, 2-Me), 2.60 (3 H, s, 6-Me), 4.37 (2 H, q, *J* 8, CH_2CH_3) and 7.78 (1 H, s, 3-H); *m/z* 224 (M^+, 100%); ν_{max}/cm^{-1} 1685.

The reagent **3b** and 2-aminothiazole **1A** gave *ethyl 6-phenylimidazo*[2,1-b]*thiazole-5-carboxylate* **10Ab** (64%), m.p. 69–71 °C (CH_2Cl_2–light petroleum) (Found: C, 61.8; H, 4.35; N, 10.3 $C_{14}H_{12}N_2O_2S$ requires C, 61.8; H, 4.35; B, 10.3%); δ_H 1.33 and 4.37 (Et), 7.45 (3 H, m, Ph), 7.86 (2 H, m, Ph), 7.00 (1 H, d, *J* 5.1, 2-H) and 8.23 (1 H, d, *J* 5.1, 3-H).

The reagent **3b** and 2-amino-4-methylthiazole **1C** gave *ethyl 3-methyl-6-phenylimidazo*[2,1-b]*thiazole-5-carboxylate* **10Cb** (61%), m.p. 86–88 °C (CH_2Cl_2–light petroleum) (Found: C, 63.2; H, 4.8; N, 9.8. $C_{15}H_{14}N_2O_2S$ requires C, 62.9; H, 4.9; N, 9.8); δ_H include 2.66 (3 H, s, 3-Me) and 6.53 (1 H, s, 2-H).

The reagent **3b** and 2-amino-5-benzylthiazole **1D** gave *ethyl 2-benzyl-6-phenylimidazo*[2,1-b]*thiazole-5-carboxylate* **10Db** (64%), m.p. 101–102 °C (CH_2Cl_2–light petroleum) (Found: C, 69.7; H, 5.0; N, 7.6. $C_{21}H_{18}N_2O_2S$ requires C, 69.6; H, 5.0; N, 7.7%); δ_H include 4.12 (2 H, s, CH_2Ph) and 7.94 (1 H, s, 3-H).

Conversion of the Esters **10** *into the Imidazothiazoles* **13**.—A solution of the ester **10Aa** (0.51 g) and KOH (0.65 g) in EtOH (10 cm^3)–water (1 cm^3) was boiled under reflux for 2 h. Aq. HCl (5 mol dm^{-3}; 20 cm^3) was added, and the boiling was continued for a further 2 h. The solution was cooled, and basified with aq. NH_3 (18 mol dm^{-3}). Extraction with CH_2Cl_2 gave a product (0.27 g), b.p. 121–123 °C (bath temp.), 3 mmHg, identified as 6-methylimidazo[2,1-*b*]thiazole **13Aa** by spectrometric comparison with an authentic specimen.[2]

Similarly the ester **10Ab** gave 6-phenylimidazo[2,1-*b*]thiazole **13Ab** (85%), m.p. and mixed[2] m.p. 146–147 °C. The ester **10Cb** gave 3-methyl-6-phenylimidazo[2,1-*b*]thiazole **13Cb** (84%), m.p. and mixed[2] m.p. 112–113 °C.

The ester **10Db** (0.56 g) gave a product (0.33 g) identical with authentic 2-benzyl-6-phenylimidazo[2,1-*b*]thiazole **13Db** obtained by the following synthesis which was carried out under the general conditions.[2]

Treatment of 2-amino-5-benzylthiazole **1D** (0.51 g) with phenacyl bromide (0.53 g) gave *2-amino-3-benzoylmethyl-5-benzylthiazolium bromide* (0.95 g), m.p. 178–180 °C (MeOH) (Found: C, 55.2; H, 4.4; N, 7.1. $C_{18}H_{17}BrN_2OS$ requires C, 55.5; H, 4.4; N, 7.2%). Cyclisation of this salt followed by basification afforded the *thiazole* **13Db** (0.61 g), m.p. 174–175 °C ($CHCl_3$–

light petroleum) (Found: C, 74.3; H, 4.7; N, 9.5. $C_{18}H_{14}N_2S$ requires C, 74.4; H, 4.9; N, 9.65%); δ_H include 7.62 (1 H, s, 5-H); *m/z* 290 (M^+, 100%).

The Esters **11** *and* **14**.—Procedure A with diethyl bromomalonate **4** (6.38 g) and 2-aminothiazole **1A** (2.67 g) in dry Me_2CO (15 cm^3), and collection of the precipitated material gave a salt (9.45 g) [m.p. 165–167 °C; δ_H 1.36 (6 H, t, *J* 7.1) and 4.39 (4 H, q, *J* 7.1, two Et), 1.75 (6 H, s, two Me), 6.82 (1 H, d, *J* 5.0, 2-H) and 7.28 (1 H, d, *J* 5.0, 3-H)] formulated as 5,5-di(ethoxycarbonyl)-5,5-dimethyl-5,6-dihydro-7*H*-imidazo-[2,1-*b*] thiazolium bromide. Basification of this salt afforded *5,5-di(ethoxycarbonyl)-6,6-dimethyl-5,6-dihydroimidazo*[2,1-b]-*thiazole* **11** as a yellow oil (6.44 g), b.p. 139–141 °C, 0.02 mmHg (Found: C, 52.0; H, 6.2; N, 9.2. $C_{13}H_{18}N_2O_4S$ requires C, 52.3; H, 6.1; N, 9.4%); δ_H 1.32 (6 H, t, *J* 7.0), 4.29 (4 H, q, *J* 7.0, two Et), 1.44 (6 H, s, two Me), 5.84 (1 H, d, *J* 5.1, 2-H) and 6.60 (1 H, d, *J* 5.1, 3-H); ν_{max}/cm^{-1} 1743 and 1728.

A solution of the foregoing product **11** (1.11 g) and KOH (1.12 g) in EtOH (20 cm^3)–H_2O (2 cm^3) was boiled under reflux for 2 h. Aq. HCl (5 mol dm^{-3}; 40 cm^3) was added, the boiling was continued for a further 2 h, and the solution was then evaporated to dryness at 100 °C, 15 mmHg. The residue was dissolved in MeOH (60 cm^3)–H_2SO_4 (2 cm^3), and the solution was boiled under reflux for 3 h. Water (120 cm^3) was added, and the solution was basified with solid $NaHCO_3$. Extraction with CH_2Cl_2 gave *methyl 6,6-dimethyl-5,6-dihydroimidazo*[2,1-b]-*thiazole-5-carboxylate* **14** (0.58 g), b.p. 136–140 °C (bath temp.), 0.03 mmHg (Found: C, 50.8; H, 5.4; N, 13.3. $C_9H_{12}N_2O_2S$ requires C, 50.9; H, 5.7; N, 13.2%); δ_H 1.23 (3 H, s) and 1.53 (3 H, s) (CMe_2), 3.80 (3 H, s, CO_2Me), 4.30 (1 H, s, 5-H), 5.77 (1 H, d, *J* 4.8, 2-H) and 6.43 (1 H, d, *J* 4.8, 3-H); ν_{max}/cm^{-1} 1738.

Formation of the 2-Amidothiazoles **12**.—The 2-aminothiazoles and the reagents (**5**, **6**, **7**) were used in procedure A or B, and the materials so obtained were basified. The structures of the products were confirmed by spectrometric examination.

The amine **1A** and reagent **5** (procedure A) gave 2- acetamidothiazole **12Ac** (69%), m.p. 210–211 °C (from CH_2Cl_2–light petroleum) (lit.,[12] 205–206 °C). Amine **1B** and reagent **5** (procedure A) gave 2-acetamido-5-methylthiazole **12Bc** (71%), m.p. 233–235 °C (EtOH) (lit.,[13] 225 °C). Amine **1A** and reagent **6** (procedure B) gave 2-benzamidothiazole **12Ad** (68%), m.p. 150–151 °C (CH_2Cl_2–light petroleum) (lit.,[15] 149 °C). Procedure A with 2-aminothiazole (0.66 g) and *p*-nitrophenyl iodoacetate **7** (2.02 g) gave a yellow precipitate which was collected and basified (at 0 °C for 5 min). Work-up of the combined CH_2Cl_2 solutions, and evaporation of the solvent at 0 °C, 15 mmHg gave a product (1.01 g) formulated as 2-*N*-iodoacetylaminothiazole **12Ae**, m.p. 159–161 °C (decomp.); δ_H 3.88 (2 H, s, CH_2), 7.15 (1 H, d, *J* 3.5, 5-H) and 7.48 (1 H, d, *J* 3.5, 4-H); *m/z* 268 (M^+, 10%) and 100 ($M - COCH_2I + H^+$, 100), which decomposed during attempted crystallisation.

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