Tautomerism in 2-Trichloro- and 2-Trifluoro-acetamidothiazoles

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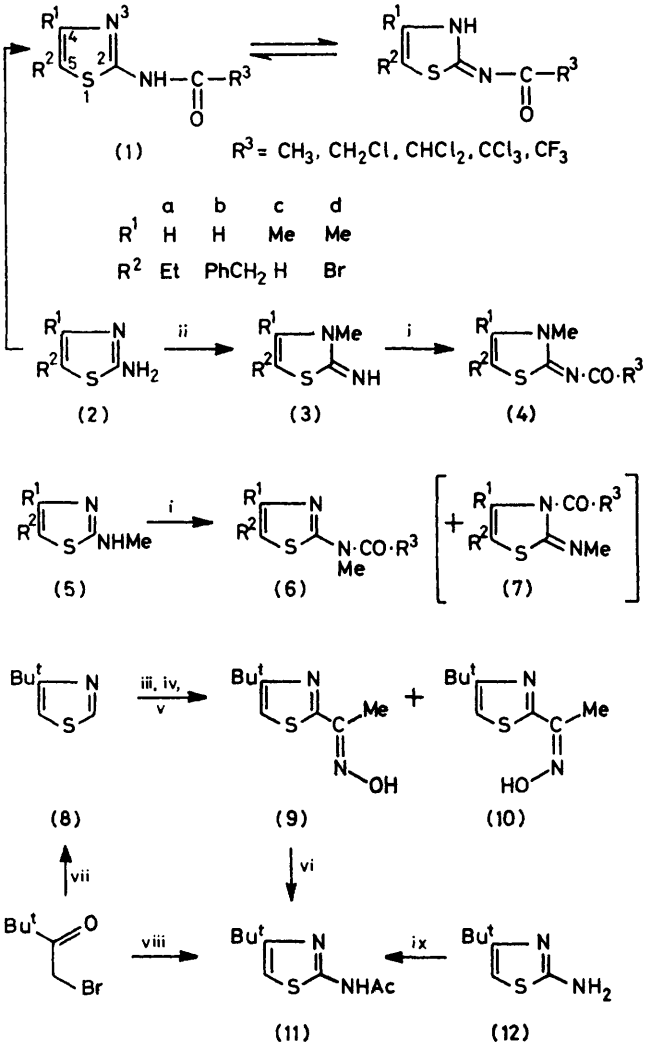
Series of new 4- and 5-substituted thiazoles with acetamido-, mono-, di-, and tri-chloroacetamido-, and trifluoroacetamido-groups at position 2 have been prepared. Amide-acylimine tautomerism in these compounds has been investigated by comparing their i.r. and u.v. spectra in carbon tetrachloride and in acetonitrile with those of related 2-*N*-methylacetamido- and 3-methyl-2-acetylimino-thiazoles. The trichloro- and trifluoro-acetamides exhibit tautomerism in both solvents; the acylimino-forms are most stable with the trifluoro-compounds in the more polar solvent.

THE main object of this work was to examine potentially tautomeric 2-halogenoacetamidothiazoles. These compounds are formed from 2-aminothiazoles (Scheme), and for the work to be soundly based it is necessary to be certain that acylation normally involves the 2-amino-group and gives the 2-acylamino-compounds (1) rather than the ring nitrogen thereby leading to 2-imino-3-acyl-Δ^4-thiazolines [as structure (7) but with =NH at position 2]. Protonation of 2-aminobenzothiazoles [1] and 2-aminothiazoles,[2] and methylation of the latter,[3] occur preferentially at the ring nitrogen, and trifluoroacetylation of some 2-methylaminothiazoles gives both types of product.[4] That acetylation of 2-aminothiazoles leads to 2-acetamido-compounds was first established rigorously in the 4-phenyl series, largely by u.v.[5a] and, later, n.m.r. studies,[5b] and it was shown that this almost certainly applies to 2-amino- and 2-amino-4-methylthiazole. However, since the present study was to depend on spectrometric methods for distinguishing between tautomeric forms it was considered prudent to establish the correctness of the underlying structures by an independent chemical approach to one 2-aminothiazole (12).

For this purpose 4-t-butylthiazole (8) was converted into its 2-acetyl derivative and thence into a mixture of diastereoisomeric oximes (9) and (10) which were separated by preparative layer chromatography. Beckmann rearrangement of the mixture and of the major oxime gave a product which, since it was also obtained by acetylating the 2-amine (12) and by a Hantzsch synthesis using bromopinacolone and *N*-acetylthiourea, must be 4-t-butyl-2-acetamidothiazole (11). [Neither of the oximes showed intramolecular O–H · · · N(3) bonding, which is possible in a rotamer of the *Z*-oxime (10). The preference for the form shown and the absence of bonding parallel the behaviour of the corresponding benzil monoxime.[6] Formulation of the major isomer as the *E*-oxime (9), on the basis of its rearrangement, is not required for the present argument.] Compounds (1a—d; $R^3 = CH_3$) share the characteristic spectrometric properties of the amide (11) and are thus 2-acetamidothiazoles.

Although almost all the potentially tautomeric amides (1), and the spectrometric reference compounds (4) and (6), are new the preparative work was straightforward and requires little comment. The 5-bromo-2-amine (2d), which is unstable, was liberated from its hydrobromide and used immediately in acylations; decomposition occurred during attempted methylations



SCHEME

Reagents: i, $(R^3CO)_2$ for $R^3 = CH_3$, CF_3; R^3COCl for others; ii, MeI, then KOH; iii, Bu^nLi; iv, $MeCONMe_2$; v, H_2NOH; vi, PCl_5–Et_2O, then H_2O; vii, $HCSNH_2$; viii, $AcNH{\cdot}CS{\cdot}NH_2$; ix, Ac_2O

thus preventing preparation of reference compounds (4d). Trifluoroacetylation of the 2-methylaminothiazoles at 20 °C occurred, as expected, on the exocyclic nitrogen giving the 2-trifluoroacetylamido-compounds but at higher temperature these were accompanied by minor products. Separation of the mixtures obtained from two amines (5a) and (5d) led to the isolation of the standard amides (6; $R^3 = CF_3$) and the 2-methylimino-3-trifluoroacetyl-Δ^4-thiazolines (7; $R^3 = CF_3$).

Previous spectrometric studies by Sheinker and co-workers [7] established that acetyl and halogenoacetyl derivatives of 2-aminothiazole (1; $R^1 = R^2 = H$), as solids, may adopt either the amide or the imine form, and that solutions of certain derivatives contain both forms. Thus, from the i.r. spectra of mulls it was concluded that the compounds with $R^3 = CH_3$ and $CHCl_2$ exist as amides (*A*) and those with $R^3 = CCl_3$ and CF_3 as substituted imines (*I*); from u.v. examinations (discussed later) values were obtained for the tautomeric equilibrium constants of the compounds with $R^3 = CHCl_2$ and CCl_3.[7a] Subsequently, mass spectral investigations, which allow the ratio of forms for the phase being vaporised to be inferred, indicated the presence of the *I* form in the dichloro-derivative $R^3 = CHCl_2$.[7b]

Carbon tetrachloride and acetonitrile were used as solvents in the present study; this pair differ appreciably in polarity and are suitable for making direct comparisons between i.r. and u.v. spectra as shown in Table 1. Since the spectra of the amides (1) and the reference compounds with $R^3 = CH_3$, CH_2Cl and $CHCl_2$ differed little between the four Series (a—d) only one set of results [Series (a), Section 1 of Table 1] is reported here. Sections 2 and 3 contain the results from the trichloro- and trifluoroacetamidothiazoles (which do exhibit tautomerism) of all the series.

Since the reference compounds (4a) and (6a) have markedly different u.v. absorptions which are little influenced by the polarity of the solvent this technique can be used for detecting tautomerism in the amides and establishing the structures of the predominant forms. On the reasonable assumption that methylation of the exocyclic nitrogen and chlorination of the acetyl

TABLE 1

Spectra of 2-acetamidothiazoles and reference compounds

Compound	R^3	I.r. C=O absorptions (cm^{-1})		U.v. bands (nm)	
		CCl_4	MeCN	CCl_4	MeCN
Section 1					
(1a)	CH_3	1 703(530) *	1 693(430)	271(8 100)	269(8 000)
(1a)	CH_2Cl	1 693(540)	1 695(410)	276(8 600)	274(8 100)
(1a)	$CHCl_2$	1 707(330) 1 692(170)	1 709(280 1 692(120)	284(8 700)	285(8 600)
(6a)	CH_3	1 674(550)	1 667(460)	275(8 500)	273(8 400)
(4a)	CH_3	1 612(380)	1 601(310)	302(13 000)	302(11 900)
Section 2					
(1a)	CCl_3	1 721/1 645[17 : 1] †	1 709/1 628[1 : 2.6]	289(8 100)	314(11 500)
(1b)	CCl_3	1 722/1 644[*ca.* 25 : 1]	1 710/1 630[1 : 2.1]	287(8 100)	314(12 100)
(1c)	CCl_3	1 719/1 648[*ca.* 20 : 1]	1 712/1 634[1 : 2.2]	286(7 700)	312(11 000)
(1d)	CCl_3	1 719/—	1 708/1 633(1.5 : 1]	297(7 500)	310(7 600)
(6a)	CCl_3	1 685(630)	1 679(460)	291(8 000)	289(7 800)
(6b)	CCl_3	1 685(680)	1 680(530)	290(8 200)	288(8 100)
(6d)	CCl_3	1 681(650)	1 675(530)	299(8 000)	297(7 600)
(4a)	CCl_3	1 635(420)	1 625(350)	313(14 500)	314(13 600)
(4b)	CCl_3	1 629(380)	1 623(360)	314(14 100)	314(13 700)
Section 3					
(1a)	CF_3	1 737/1 652[3.5 : 1]	1 722/1 635[1 : 4.4]	292(8 100)	308(11 000)
(1b)	CF_3	1 738/1 654[4.1 : 1]	1 722/1 636[1 : 3.6]	288(8 200)	308(11 500)
(1c)	CF_3	1 739/1 652[3.6 : 1]	1 728/1 637[1 : 4.2]	289(7 600)	308(11 300)
(1d)	CF_3	1 737/—	1 727/1 638[1.1 : 1]	292(7 800)	307(7 800)
(6a)	CF_3	1 700(760)	1 695(690)	286(7 800)	282(7 600)
(6b)	CF_3	1 701(810)	1 695(710)	284(7 900)	282(7 800)
(6c)	CF_3	1 703(800)	1 697(710)	286(7 300)	284(7 200)
(6d)	CF_3	1 699(820)	1 693(720)	295(7 900)	292(7 400)
(4a)	CF_3	1 642(510)	1 630(470)	309(13 500)	209(12 400)
(4b)	CF_3	1 642(520)	1 630(510)	308(13 900)	310(13 500)
(4c)	CF_3	1 641(510)	1 632(490)	309(13 600)	309(13 200)
(7a)	CF_3	1 642(580)	1 630(560)	302(9 100)	310(11 300)

Section 4

Values of the equilibrium constant K = [Imine form]/[Amine form] at 303 K

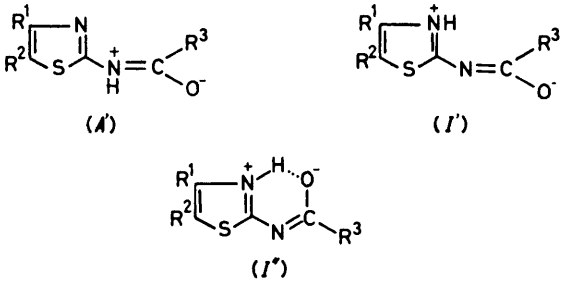
		(1a)	(1b)	(1c)	(1d)
$R^3 = CCl_3$	CCl_4	0.09	*ca.* 0.07	*ca.* 0.08 [a]	*ca.* 0
	MeCN	3.5	3.1	3.1 [a]	0.9 [a]
$R^3 = CF_3$	CCl_4	0.42	0.38	0.44	*ca.* 0
	MeCN	6.5	5.0	6.1	1.3 [b]

* Molecular extinction coefficients in parentheses. † Relative absorbances of the tautomeric forms in square brackets. [a] Calculated using averages of i.r. values of compounds (4) and (6) in Series (a) and (b). [b] Calculated using i.r. values of compounds (4) and (6) in Series (c).

group of the amide (1a; $R^3 = CH_3$) cause modest bathochromic shifts, compounds (1a; $R = CH_3$ and CH_2Cl) are seen to adopt the *A* (amide) form in both carbon tetrachloride and acetonitrile. With the dichloro-compound (1a; $R^3 = CHCl_2$) an increase in the solvent polarity leads to a small shift to longer wavelength rather than the reverse which was observed with the previous amides and the reference compound (6a; $R = CH_3$); the presence of some *I* (imine) form in acetonitrile is thus suggested but (see later) the amount of this tautomer must be very small.

The u.v. spectra of the trichloroacetamidothiazoles (1a—c; $R^3 = CCl_3$) provide strong evidence for the predominance of *A* forms in carbon tetrachloride and of *I* forms in acetonitrile. With the trifluoro-compounds (1a—c; $R^3 = CF_3$) the position in carbon tetrachloride is more balanced while in acetonitrile there is a very marked preference for the *I* forms. The absence of reference compounds in Series (d) prevents such clear interpretation but it appears that the 5-bromo-substituent reduces the relative amounts of the *I* forms of compounds (1d; $R^3 = CCl_3$ and CF_3). Although there should be an appreciable separation (*ca.* 25 nm) between the absorption maxima of the *A* and *I* forms of the tautomeric amides all the experimental traces were so nearly symmetrical that curve resolution was not feasible and tautomeric equilibria constants could not be calculated without crude approximations being made. The data from the reference compounds suggest that the *I* form of a tautomeric pair will have the higher extinction coefficient; an equilibrium constant based on the position of a composite maximum will thus be biased in favour of the imine-tautomer. It is difficult to see how equilibrium constants were obtained so precisely (to three significant figures) from the published u.v. spectra.[7a]

Since the carbonyl bands of related reference compounds (4) and (6) are well separated (*ca.* 55 cm^{-1}) and those of *A*–*I* pairs are even further apart (*ca.* 75 cm^{-1}) i.r. spectrometry was used for the quantitative study of the tautomeric equilibria. To reduce errors arising from the general difficulty (absence of figures for the extinction coefficients of the tautomers) it was assumed that the *ratio* of the extinction coefficients of an *A*–*I* pair is equal to that of the related pair of reference compounds (6)–(4). These ratios, together with the relative absorbances of the carbonyl bands in the spectra of the tautomeric amides, led to the equilibrium constants in Section 4 of Table 1. [In view of the uncertainties inherent in this approach the use of band areas rather than absorbances did not appear worthwhile. The positions and separations of the components of the doublets observed with the dichloroacetamide (1a) show that these bands arise from rotational isomerism. Despite the indications from u.v. spectrometry that the solution in acetonitrile contains some *I* form no absorption at *ca.* 1 625 cm^{-1} could be detected.] From the *K* values the relative stability of the *I* form is seen to increase as the acetyl group is progressively chlorinated, or as the halogen in the trihalogenoacetyl group is changed from chlorine to fluorine, or as a 5-bromo-substituent is replaced by hydrogen, or as the solvent becomes more polar. The first two effects probably arise from the accompanying decrease in the basicity of the exocyclic nitrogen of the *A* form, protonation at the ring nitrogen (*i.e.* formation of the *I* form) hence becoming more favourable. Conversely a 5-bromo-substituent reduces the basicity of the ring nitrogen. The difference between the positions of the bands of an *A*–*I* pair is greater than would be predicted on the basis that the *I* form is formally an extended conjugated amide. A larger contribution of a dipolar canonical form (*I'* or *I''*, in Figure) to the *I* form



than that of canonical *A'* to the *A* form is to be expected, since this restores aromaticity to the heterocyclic ring. Comparison of the bands of the *I* forms and those of the ring-*N*Me imines (4) excludes the chelated structure *I''* for the dipolar canonical form. Increasing solvent polarity should result in a still larger contribution of the canonical form *I'*: the consequential preference for the *I* forms is consistent with the greater shifts observed in the positions of their absorptions (relative to those of the *A* forms) as the solvent is changed from carbon tetrachloride to acetonitrile.

EXPERIMENTAL

General directions were as described in *J. Chem. Soc. C*, 1968, 2674 except that the ^1H n.m.r. spectra (in $CDCl_3$) were recorded at 90 MHz. The procedures reported here for compounds (1)—(7) in Series (a) were used in other series; the characterisation of all the new compounds involved in this section of the work is shown in Table 2. The preparations of compounds (8)—(12) are reported in the standard manner.

The Amides (1a).—Ac_2O (1.4 ml) was added during 10 min to a solution of 2-amino-5-ethylthiazole [8] (1.55 g) in $CHCl_3$ (15 ml) which was boiling under reflux, and the boiling was continued for a further 1.5 h. The solution was poured into ice–H_2O (15 ml), and basified with Na_2CO_3. Isolation with EtOAc, absorption on SiO_2, elution with light petroleum (b.p. 60—80 °C)–Et_2O (4 : 1), and crystallisation from EtOAc–light petroleum gave the *amide* (1a; $R^3 = CH_3$) (1.43 g). Similarly $CH_2Cl{\cdot}COCl$ (0.8 ml) and 2-amino-5-ethylthiazole (1.02 g) gave, after boiling under reflux for 2 h, the *monochloroacetylamide* (1a; $R^3 = CH_2Cl$) (0.91 g). Similarly $CHCl_2{\cdot}COCl$ (0.9 ml) and 2-amino-5-ethylthiazole (1.06 g) gave, after boiling under reflux for 2.5 h, the *dichloroacetylamide* (1a; $R^3 = CHCl_2$) (1.37 g). Similarly $CCl_3{\cdot}COCl$ (1.1 ml) and 2-amino-5-ethylthiazole (1.02 g) gave, after boiling under reflux for 2.5 h, the *trichloroacetylamide* (1a; $R^3 = CCl_3$) (1.17 g). Similarly $(CF_3CO)_2O$ (1.3 ml

and 2-amino-5-ethylthiazole (1.03 g) gave, after boiling under reflux for 2 h, the *trifluoroacetylamide* (1a; $R^3 = CF_3$) (1.1 g).

The Acylimines (4a).—MeI (1.75 ml) was added during 5 min to 2-amino-5-ethylthiazole (3.35 g) which was stirred at 20 °C, and the mixture was heated at 40 °C under reflux for 1 h. The solid which formed was collected and crystallised from Pr^iOH to give *5-ethyl-3-methyl-Δ^4-thiazolin-2-ylidenium iodide* (5.1 g). A solution of this salt (4.51 g) in H_2O (20 ml) was basified with 1M-NaOH. Isolation with EtOAc afforded an oil (2.3 g) which was distilled at 0.4 mmHg to give the *imine* (3a) (1.3 g).

AcCl (1.1 ml) was added during 10 min to a solution of the imine (3a) (0.61 g) in $CHCl_3$ (25 ml) which was boiled under reflux during the addition and then for a further 2 h. Work-up as described for the amides (1a) afforded an oil (0.8 g) which was distilled at 96—97 °C/0.01 mmHg to give the *acetylimine* (4a; $R^3 = CH_3$) (0.53 g). Similarly CCl_3COCl (0.7 ml) and the imine (3a) (0.85 g) afforded, after boiling under reflux for 2.5 h, a solid (1.6 g) which was sublimed at 0.1 mmHg to give the *trichloroacetylimine* (4a; $R^3 = CCl_3$) (1.38 g). Similarly $(CF_3CO)_2O$ (2 ml) and the imine (3a) (1 g) afforded, after boiling under reflux for 2.5 h, a solid (1.6 g) which was sublimed at 1.5 mmHg to give the *trifluoroacetylimine* (4a; $R^3 = CF_3$) (1.45 g).

The 2-N-*Methylamine* (5a) *and Derivatives* (6a) *and* (7a).—A solution of 2-bromobutanal (9.9 g) in dioxan (5.1 g) was added to a solution of *N*-methylthiourea (5.9 g) in EtOH (100 ml), and the solution was boiled under reflux for 3 h. Evaporation at 100 °C/20 mmHg, addition of H_2O (80 ml), basification with 18M-NH_3, and extraction with $CHCl_3$ gave an oil (9.3 g). Two distillations afforded a fraction with b.p. 69—72 °C/0.1 mmHg which was dissolved in EtOAc and passed through SiO_2. Evaporation and a further distillation gave the 2-N-*methylamine* (5a) (4.6 g).

Treatment of the amine (5a) (1 g) with CCl_3COCl (0.9 ml) [as described for the imine (3a)] afforded an oil (1.8 g). This was distilled at 0.1 mmHg and further purified by adsorption onto SiO_2 and elution with light petroleum–Et_2O (1 : 9) to give the N-*methyltrichloroacetamide* (6a; $R^3 = CCl_3$) (1.1 g).

$(CF_3CO)_2O$ (0.5 ml) was added during 3 min to a solution of the amine (5a) (0.33 g) in $CHCl_3$ (20 ml) at 20 °C, and the solution was heated at 40 °C under reflux for 1 h. Work-up afforded a solid (0.45 g) which was eluted from SiO_2 with light petroleum–Et_2O (1 : 3) and sublimed at 0.05 mmHg to give the N-*methyltrifluoroacetamide* (6a; $R^3 = CF_3$) (0.24 g). $(CF_3CO)_2O$ (1.1 ml) was added during 5 min to a solution of the amine (5a) (1 g) in $CHCl_3$ (30 ml) which was boiled under reflux during the addition and then for a further 2.5 h. Work-up afforded an oil (1.3 g) which was distilled at 0.1 mmHg, adsorbed onto SiO_2, and eluted with light petroleum–EtOAc (1 : 9) to give the *3-trifluoroacetylthiazoline* (7a; $R^3 = CF_3$) (0.16 g).

4-t-Butylthiazole * (8).—P_2S_5 (4.9 g) was added to a stirred mixture of 1-bromo-3,3-dimethylbutan-2-one (10 ml) and $HCONH_2$ (4 ml) which was cooled in an ice–salt bath. The ice was allowed to melt and the temperature of the slurry rose until, at *ca.* 5 °C, an exothermic reaction occurred. The stirred mixture was heated at 90 °C for 1 h, cooled, diluted with H_2O (50 ml), and basified with 18M-NH_3. Isolation with EtOAc gave 4-t-butylthiazole (4.7 g), b.p. 54—55 °C/14 mmHg (Found: C, 59.6; H, 7.8; N, 9.6; S, 22.9. Calc. for $C_7H_{11}NS$: C, 59.5; H, 7.9; N, 9.9; S, 22.7%); τ 1.27 (d, *J* 2 Hz, 2-H), 3.08 (d, *J* 2 Hz, 5-H), and 8.63 (s, Bu^t); *m/z* 141 (M^+, 23%) and 126 (100).

The Oximes (9) *and* (10).—A solution of 4-t-butylthiazole (1.41 g) in dry hexane (10 ml) was added during 20 min to a 0.59M-solution of Bu^nLi in hexane (17.5 ml) which was stirred under N_2 at −70 °C during the addition and for a further 45 min. $MeCONMe_2$ (2 ml) was added during 10 min, and stirring was continued for a further 30 min. The stirred mixture was allowed to attain room temperature, then poured into ice–water (50 g) containing $NaHCO_3$ (1 g). Isolation with Et_2O afforded *2-acetyl-4-t-butylthiazole* (0.97 g), b.p. 48—52 °C/0.1 mmHg (Found: C, 58.9; H, 7.1; N, 7.6; S, 17.6. $C_9H_{13}NOS$ requires C, 59.0; H, 7.2; N, 7.6; S, 17.5%); τ 2.76 (s, 5-H), 7.30 (s, Ac), and 8.62 (s, Bu^t); *m/z* 183 (M^+, 33%) and 178 (100). A solution of this ketone (2.2 g), $NH_2OH{\cdot}HCl$ (1.67 g), and NaOAc (3.3 g) in H_2O–EtOH (14 ml; 1 : 1 v/v) was boiled under reflux for 3 h. Work-up gave an oil (1.95 g) shown by ^1H n.m.r. to contain a mixture of oximes in the ratio 5 : 1. Preparative layer chromatography [SiO_2; single development with light petroleum (b.p. 30—40 °C)–Et_2O (1 : 1)] of the mixture (1 g) gave both (E)-*4-t-butyl-2-(1-hydroxyiminoethyl)thiazole* (9) (0.62 g), m.p. 72—79 °C (Found: C, 54.6; H, 7.0; N, 14.0; S, 15.9. $C_9H_{14}N_2OS$ requires C, 54.6; H, 7.1; N, 14.1; S, 16.2%); τ 1.73 (1 H, br, OH), 3.16 (s, 5-H), 7.59 (s, Me), and 8.66 (s, Bu^t); $\nu_{max.}$ (10^{-3}M in CCl_4) 3 592 cm^{-1}, only band in OH region; *m/z* 198 (M^+, 100%) and the (Z)-*oxime* (10) (75 mg), m.p. 115—119 °C (Found: *m/z* 198.0826. $C_9H_{14}N_2OS$ requires M^+ 198.0827); τ *ca.* −2 (1 H, br, OH), 2.89 (s, 5-H), 7.59 (s, Me), and 8.63 (s, Bu^t); $\nu_{max.}$ (5×10^{-4}M in CCl_4) 3 593 cm^{-1}, only band in OH region; *m/z* 198 (M^+, 100%). The oximes equilibrated in 2 h on a SiO_2 plate.

2-Acetamido-4-t-butylthiazole (11).—(*a*) PCl_5 (finely powdered; 0.64 g) was added in portions to a stirred solution of the mixture of oximes (9) and (10) (ratio 5 : 1; 0.5 g) in dry Et_2O (10 ml). The stirred mixture was heated on a steam bath until the solvent evaporated, and then for a further 10 min after which it was diluted with H_2O (10 ml) and the mixture boiled under reflux for 5 min; it was then cooled and filtered. The filtrate was neutralised with saturated aqueous $NaHCO_3$, and the precipitate was purified by preparative layer chromatography [SiO_2; development with light petroleum–Et_2O (1 : 1)] to give 2-acetamido-4-t-butylthiazole (0.19 g), m.p. 180—182 °C (from MeOH–H_2O) (lit.,[9] 175—176 °C) (Found: C, 54.6; H, 7.0; N, 14.1. Calc. for $C_9H_{14}N_2OS$: C, 54.5; H, 7.1; N, 14.1%); τ 0.80 (1 H, br, NH), 3.49 (s, 5-H), 7.76 (s, Ac), and 8.73 (s, Bu^t); $\nu_{max.}$ (CCl_4) 1 708 cm^{-1} (ε 560); ν(MeCN) 1 696 cm^{-1} (470); *m/z* 198 (M^+, 22%) and 141 (100). Similar treatment of the (*E*)-oxime (9) (70 mg) with PCl_5 (100 mg) gave the amide (11) (20 mg). ^1H N.m.r. examination of the material obtained by treating the (*Z*)-oxime (10) (50 mg) with PCl_5 (70 mg) did not reveal the presence of the amide (11).

(*b*) A solution of 2-amino-4-t-butylthiazole [9] (12) (1 g) in Ac_2O (10 ml) was boiled under reflux for 1 h. Work-up gave the amide (11) (0.91 g), m.p. 180—182 °C [undepressed by admixture with the product from procedure (*a*)].

(*c*) 1-Bromo-3,3-dimethylbutan-2-one (3.4 ml) was added during 10 min to a solution of *N*-acetylthiourea (2.95 g) in EtOH (25 ml) which was boiled under reflux during the

* The citations (*e.g.*, J. Chouteau, C. Davidovics, J. Metzger, M. Azzaru, and M. Poits, *Bull. Soc. Chim. Fr.*, 1962, 1794) of this compound refer to a Thesis (M. Carrega, Marseilles). Preparative details and characterisation do not appear to have been published.

TABLE 2

Characterisation of new compounds (1)—(7) and some intermediates

Compound	M.p. (°C)	B.p. (°C)/ mmHg	Analyses (%) Found C	H	N	Found *m/z*	Molecular formula	Required C	H	N	M^+
(1a; $R^3 = CH_3$)	147—149		49.4	5.9	16.5		$C_7H_{10}N_2OS$	49.4	5.9	16.5	
(1a; $R^3 = CH_2Cl$)	151—153		41.2	4.3	13.8		$C_7H_9ClN_2OS$	41.1	4.4	13.7	
(1a; $R^3 = CHCl_2$)	177—179		35.3	3.3	11.7		$C_7H_8Cl_2N_2OS$	35.2	3.4	11.7	
(1a; $R^3 = CCl_3$)	196—198		30.8	2.8	10.4		$C_7H_7Cl_3N_2OS$	30.7	2.6	10.2	
(1a; $R^3 = CF_3$)	150—152		37.5	3.3	12.7		$C_7H_7F_3N_2OS$	37.5	3.15	12.5	
5-Ethyl-3-methyl-Δ^4-thiazolin-2-ylidenium iodide	158—160		26.9	4.2	10.4		$C_6H_{11}IN_2S$	26.7	4.1	10.4	
(3a)		100—101/0.4	50.9	7.2	19.5		$C_6H_{10}N_2S$	50.7	7.1	19.7	
(4a; $R^3 = CH_3$	52—55		52.0	6.5	15.2		$C_6H_{12}N_2OS$	52.1	6.6	15.2	
(4a; $R^3 = CCl_3$)	76—77		33.8	3.4	9.7		$C_8H_9Cl_3N_2OS$	33.4	3.15	9.7	
(4a; $R^3 = CF_3$)	77—79		40.5	3.9	1.55		$C_8H_9F_3N_2OS$	40.3	3.8	11.8	
(5a)		70—72/0.1				142.0565					142.0565
(6a; $R^3 = CH_3$)	31—33	86—88/0.05	52.05	6.7	15.2		$C_8H_{12}N_2OS$	52.1	6.6	15.2	
(6a; $R^3 = CCl_3$)	54—56					285.9501					285.9501
(6a; $R^3 = CF_3$)	49—50					238.0388	$C_8H_9F_3N_2OS$				238.0388
(7a; $R^3 = CF_3$)	64—66					238.0388	$C_8H_9F_3N_2OS$				238.0388
(1b; $R^3 = CH_3$)	181—183		61.8	5.1	11.9		$C_{12}H_{12}N_2OS$	62.0	5.2	12.0	
(1b; $R^3 = CH_2Cl$)	169—170		53.9	3.9	10.3		$C_{12}H_{11}ClN_2OS$	54.0	4.2	10.5	
(1b; $R^3 = CHCl_2$)	127—128		48.0	3.1	9.2		$C_{12}H_{10}Cl_2N_2OS$	47.8	3.3	9.3	
(1b; $R^3 = CCl_3$)	170—171		43.1	2.7	8.2		$C_{12}H_9Cl_3N_2OS$	42.9	2.7	8.3	
(1b; $R^3 = CF_3$)	165—167		50.5	3.1	9.7		$C_{12}H_9F_3N_2OS$	50.3	3.2	9.8	
(2b)	110—112		63.1	5.3	14.9		$C_{10}H_{10}N_2OS$	63.1	5.3	14.7	
5-Benzyl-3-methyl-Δ^4-thiazolin-2-ylidenium iodide	154—155		39.5	3.6	8.5		$C_{11}H_{13}IN_2S$	39.8	3.95	8.4	
(4b; $R^3 = CCl_3$)	109—110					347.9658	$C_{13}H_{11}Cl_3N_2OS$				347.9658
(4b; $R^3 = CF_3$)	67—69					300.0544	$C_{13}H_{11}F_3N_2OS$				300.0544
(5b)	101—102		64.4	5.8	13.6		$C_{11}H_{12}N_2S$	64.7	5.9	13.7	
(6b; $R^2 = CH_3$)	97—98		63.4	5.7	11.4		$C_{13}H_{14}N_2OS$	63.4	5.7	11.4	
(6b; $R^3 = CCl_3$)	115—116		44.7	3.1	7.9		$C_{13}H_{11}Cl_3N_2OS$	44.7	3.2	8.0	
(6b; $R^3 = CF_3$)	60—61		52.1	3.7	9.3		$C_{13}H_{11}F_3N_2OS$	52.0	3.7	9.3	
(1c; $R^3 = CH_3$)	136—137		46.4	5.0	18.0		$C_6H_8N_2OS$	46.1	5.2	17.9	
(1c; $R^3 = CH_2Cl$)	128—129		37.65	3.3	14.7		$C_6H_7ClN_2OS$	37.8	3.7	14.7	
(1c; $R^3 = CHCl_2$)	116—117		32.0	2.7	12.4		$C_6H_6Cl_2N_2OS$	32.0	2.7	12.45	
(1c; $R^3 = CCl_3$)	150—152		28.1	2.1	10.6		$C_6H_5Cl_3N_2OS$	27.8	1.9	10.8	
(1c; $R^3 = CF_3$)	152—154		34.1	2.5	13.2		$C_6H_5F_3N_2OS$	34.3	2.4	13.3	
(4c; $R^3 = CH_3$)	108—110		49.5	5.9	16.3		$C_7H_{10}N_2OS$	49.4	5.9	16.5	
(4c; $R^3 = CF_3$)	174—175		37.3	3.2	12.4		$C_7H_7F_3N_2OS$	37.5	3.15	12.5	
(5c)		110—112/0.8	46.6	6.4	21.7		$C_5H_8N_2S$	46.8	6.3	21.9	
(6c; $R^3 = CF_3$)	69—70		37.5	3.1	12.5		$C_7H_7F_3N_2OS$	37.5	3.15	12.5	
(7c; $R^3 = CF_3$)	176—177		37.4	3.1	12.4		$C_7H_7F_3N_2OS$	37.5	3.15	12.5	
(1d; $R^3 = CH_2Cl$)	145—147		27.0	2.3	10.3		$C_6H_6BrClN_2OS$	26.7	2.2	10.4	
(1d; $R^3 = CHCl_2$)	204—205		24.2	1.8	8.9		$C_6H_5BrCl_2N_2OS$	23.7	1.7	9.2	
(1d; $R^3 = CCl_3$)	107—108		21.1	1.2	8.3		$C_6H_4BrCl_3N_2OS$	21.3	1.2	8.3	
(1d; $R^3 = CF_3$)	140—141		25.0	1.4	9.7		$C_6H_4BrF_3N_2OS$	25.3	1.5	9.8	
5-Bromo-4-methylthiazol-2-ylmethylammonium bromide	205 (decomp.)		21.2	2.8	9.5		$C_5H_8Br_2N_2S$	20.9	2.8	9.7	
(6d; $R^3 = CH_3$)	111—112		34.0	3.7	11.3		$C_7H_9BrN_2OS$	33.8	3.6	11.2	
(6d; $R^3 = CCl_3$)	183—184		24.1	1.8	8.1		$C_7HBrCl_3N_2OS$	23.9	1.7	8.1	
(6d; $R^3 = CF_3$)	85—86		28.0	2.1	9.0		$C_7H_6BrF_3N_2OS$	27.7	2.1	9.2	

addition and for a further 2 h. Work-up gave the amide (11) (1.85 g), identical with the products of procedures (*a*) and (*b*).

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