Structural Features and Crystallographic Examination of 5-Acetyl- and 5-Trifluoroacetyl-2-(*N*,*N*-disubstituted amino)thiazoles

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5-Acetyl-2-(*N*,*N*-disubstituted amino)thiazoles, unsubstituted or with Me, Bu^t, or Ph groups at position 4, have been prepared by unambiguous methods and examined spectrometrically; crystallographic studies have been carried out on four of the compounds and a related 4-aryl-5-trifluoroacetylthiazole. In solution the 4-H, 4-Bu^t, and 4-Ar compounds exist predominantly in one conformation but with the 4-Me compounds, two forms (carbonyl *O,S-syn* or *anti*, related by rotation of the 5-acetyl group) of approximately equal stability are present. The *X*-ray work establishes that for 5-acetylthiazoles, as solids, the 4-H and 4-Ph derivatives have the carbonyl *O, S-syn* stereochemistry whereas the 4-Me and 4-Bu^t derivatives have the *anti* arrangement; in contrast with the 5-acetyl-4-phenyl compound the 4-aryl-5-trifluoroacetylthiazole adopts the *anti* arrangement. These findings validate a correlation, for solutions, between the stereochemistry of the rotational isomers and the positions of their i.r. CO bands.

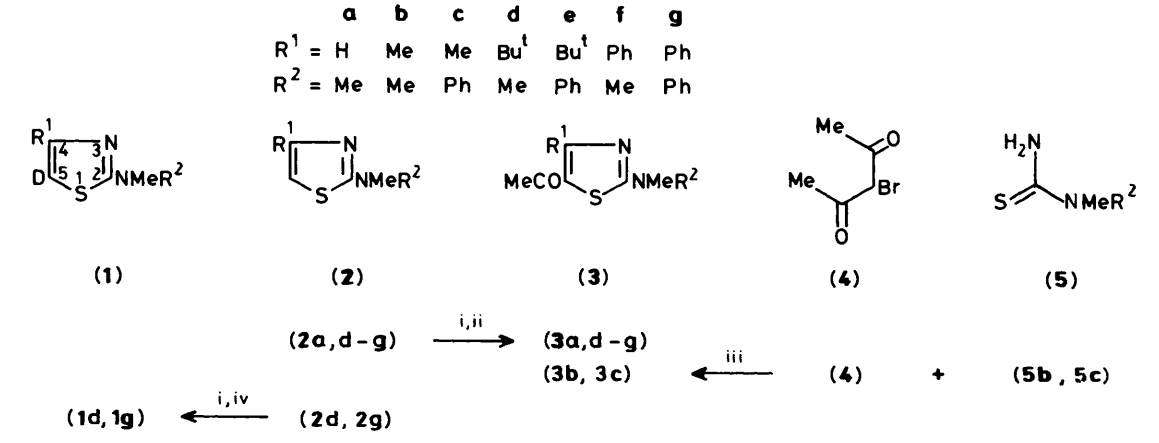
The results confirm the operation of a strong mesomeric interaction between the 2-NR_2 and 5-$CH_3(CF_3)CO$ groups.

This work is concerned mainly with the structural details of 5-acetyl-2-(*N*,*N*-disubstituted amino)thiazoles. The intention was to examine the features influenced by and therefore giving information about (i) rotational isomerism of the 5-acetyl group, and (ii) mesomeric interaction between this substituent and the 2-amino group. It was hoped also to clarify an uncertainty remaining from a previous study[1] of the corresponding 5-trifluoroacetyl compounds.

At the start of the present investigation only one 5-acetyl-2-(*N*,*N*-disubstituted amino)thiazole[2] was known; the reported preparation[3] of this compound (5-acetyl-2-morpholino-4-phenylthiazole) from an *N*-benzoyl-*N'*,*N'*-disubstituted thiourea and chloroacetone gives an isomeric product.[4] In order to avoid uncertainty about the gross structures of the compounds to be studied, they were prepared here by unambiguous routes (Scheme). The 4-methyl compounds (**3b**) and (**3c**) were obtained by Hantzsch syntheses. For the others, introduction of the acetyl group into readily available 2-(*N*,*N*-disubstituted amino)thiazole[5,6] appeared to be the most direct route. In preliminary experiments two of the starting materials (**2d**) and (**2g**) were treated with butyl-lithium and the intermediates quenched with deuterium oxide. Clean formation of the 5-deuterio-compounds (**1d**) and (**1g**) established that the intermediates are the 5-lithio derivatives. Treatment of the thiazoles (**2a**, **d**—**g**) with butyl-lithium and addition of the solutions (in tetrahydrofuran) to acetic anhydride at low temperature afforded the 5-acetyl compounds (**3a**, **d**—**g**) in yields of 72—80%.

Table 1 summarises the main features of the spectrometric examinations. The ^{1}H n.m.r. characteristics of the *N*,*N*-dimethyl and *N*-methyl-*N*-phenyl groups closely resemble those found[5] in the corresponding 5-carbaldehydes. Below *ca.* −20 °C (at a source frequency of 90 MHz) the *N*,*N*-dimethylamines exhibit two NMe signals, and the barrier to rotation about the C(2)–N bond (*ca.* 54 kJ mol^{-1}) is not significantly different from the average value (52.5 kJ mol^{-1}) of the aldehydes. Also, similarly, the *N*-methyl-*N*-phenylamino groups shows only NMe singlets, even at 180 K, and the most likely explanation is that one

Scheme. Preparation of 5-acetyl-2-(*N*,*N*-disubstituted amino)thiazoles



Reagents and conditions: i, Bu^{n}Li–THF, −70 °C, ii, Addition to Ac_2O–THF, −60 °C; iii, Me_2CO, heat; iv, D_2O, −70 °C

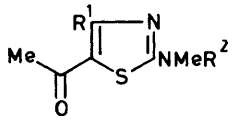
Table 1. I.r. and ^{1}H n.m.r. absorptions of 5-acetyl-2-(*N*,*N*-disubstituted amino)thiazoles (**3**)

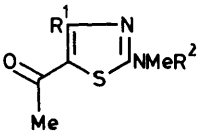
The i.r. bands (cm^{-1} at 303 K) were recorded at a spectral slit width of 1.5 cm^{-1}; for compounds (**3b**) and (**3c**) the positions of the doublets' components are followed in parentheses by their relative percentage areas. The ^{1}H n.m.r. signals (δ values at 305 K) were recorded at a source frequency of 90 MHz using solutions in $CDCl_3$; the $\Delta G^{\ddagger}$ values (kJ mol^{-1}, statistical error ±3 kJ mol^{-1}), the activation energies for rotation about the C(2)–N bond at 298 K, were obtained by examining solutions in CD_2Cl_2 over the range 180—305 K

	I.r. CO region		^{1}H n.m.r.				I.r. CO region		^{1}H n.m.r.		
Compd.	CCl_4	MeCN	*N*-CH_3	CH_3CO	$\Delta G^{\ddagger}$	Compd.	CCl_4	MeCN	*N*-CH_3	CH_3CO	$\Delta G^{\ddagger}$
(**3a**)	1 644	1 634	3.17	2.41	54	(**3d**)	1 658	1 648	3.15	2.40	
(**3b**)	1 631(53)[a]	1 621(68)	3.15	2.38[b]	55	(**3e**)	1 662	1 651	3.55	2.35	
	1 656(47)[a]	1 648(32)				(**3f**)	1 633	1 624	3.18	1.97	54
(**3c**)	1 633(36)[c]	1 624(43)	3.51	2.35[d]		(**3g**)	1 635	1 627	3.58	1.98	
	1 658(64)[c]	1 652(57)									

[a] Overtone bands (CCl_4): 3 240(45), 3 291(55). [b] Signal broadens at 189 K. [c] Overtone bands (CCl_4): 3 248(29), 3 297(71). [d] Signal broadens at 199 K; two signals (2.37 and 2.15, relative areas *ca.* 2:1) are present below 188 K.

Table 2. Correlation of CO bands (cm^{-1}, CCl_4) with conformation of the acetyl group in compounds (**3a**—**g**)





carbonyl	*O*,*S*-*syn*		carbonyl	*O*,*S*-*anti*
(**3a**)	1 644			
(**3b**)	1 631	⇌		1 656
(**3c**)	1 633	⇌		1 658
(**3f**)	1 633		(**3d**)	1 658
(**3g**)	1 635		(**3e**)	1 662

arrangement (with the phenyl group directed towards either the sulphur or the ring nitrogen atom) is adopted predominantly or exclusively.

Most of the compounds have *Me*CO signals which remain as sharp singlets over the temperature range examined. However with two compounds (**3b**) and (**3c**) the broadening at low temperature points to the presence of two forms (carbonyl *O*,*S*-*syn* and -*anti*, Table 2) arising from rotation of the acetyl group. These results could be taken to indicate that there are appreciable amounts of both rotamers in all the solutions but with barriers to interconversion so low that the present method detects rotational isomerism in only favourable cases. The i.r. examinations show, however, that there is a clear distinction between compounds (**3b**) and (**3c**) and the others. The latter have single CO bands in both CCl_4 and MeCN whereas compounds (**3b**) and (**3c**) give well-separated doublets, and the results of increasing the solvent polarity and examining the overtone region confirm the interpretation that these arise from rotational isomers. Tentative assignments of the CO bands can be made as follows. The 5-carbaldehydes adopt the *syn* arrangement;[5] conversion of an aldehyde into a methyl ketone of the same stereochemical form should be associated with a decrease (*ca.* 12 cm^{-1}) in the CO wavenumber. The bands at lower wavenumbers than those of comparable aldehydes are shown under the *O*,*S*-*syn* column of Table 2. For compounds (**3b**) and (**3c**) the higher wavenumber components of the doublets are then assigned to the *O*,*S*-*anti* forms as are the single bands (*ca.* 1 660 cm^{-1}) of the compounds (**3d**) and (**3e**) with the bulky (Bu^t) 4-substituents. Thus the nature of the 4-substituent is thought to determine which form is adopted, and only with the 4-methyl compounds in solution do the forms appear to have similar stabilities. It is apparent that this analysis would be vitiated if, for example, the various 4-substituents cause rotation of the acetyl groups out of the thiazole plane to different extents. To investigate this point and more subtle structural details four compounds (**3a**,**c**,**d**,**g**) were examined by *X*-ray diffraction, and a trifluoroacetyl-2-dimethylaminothiazole (**6**) prepared previously [1] was also studied.

The main results of the *X*-ray work are collected in Table 3 and the structures thereby established are illustrated in the Figure. [The system of atomic numbering used for presenting the results is shown in Table 3. This differs from the conventional thiazole numbering (Scheme). Thus, for example, a 4-aryl group (thiazole numbering) is attached to C(2) (atomic numbering).] Several features emerge. (*i*) The value of the angles between planes 1 and 2 show that the carbonyl groups are in, or rotated only slightly from, the plane of the thiazole ring. This tendency for coplanarity implies that there is a general preference for structural arrangements which enhance the degree of mesomeric interaction (as discussed later).

(*ii*) The 5-acetyl compounds (**3a**,**c**,**d**,**g**) differ in their preferences for the (almost) coplanar *syn* or *anti* forms. 2-(*N*,*N*-Disubstituted amino)thiazole-5-carbaldehydes,[5] the 5-acetyl compound (**3a**) lacking a 4-substituent, and (**3g**) containing a 4-phenyl group, all adopt the *syn* conformation. This preference, especially with the last compound, cannot be attributed solely to steric effects since the interference of a 4-substituent would be more severe with the methyl group of the *syn* form than with the carbonyl oxygen of the *anti* arrangement. Thus, as with other heterocyclic systems,[7] there is an intrinsic stabilisation of the carbonyl *O*, heteroatom-*syn* conformation. In the 4-phenyl compound (**3g**) several parameters undergo modification so as to accommodate the *syn* arrangement: the phenyl group is rotated by 45° out of the thiazole plane, there is some deviation from the general Me-CO-thiazole planarity, and the C(2)–C(3)–C(6) angle is bigger than that of the unperturbed *syn* form represented by compound (**3a**). Steric repulsion (4-Me—Me-CO) in the *syn* form of the 4-methyl compound (**3c**) is more severe since relief cannot be obtained by rotating the 4-substituent; the i.r. evidence that approximately equal amounts of the two forms are present in solution, agrees with there being little difference in stability between them. That the *anti* arrangement is found in the solid is, then, of little significance. Further increase in the size of the 4-substituent, as exemplified by the 4-t-butyl compound (**3d**), tips the balance decisively in favour of the *anti* form in which the accommodation afforded by an increased C(2)–C(3)–C(6) angle allows exact coplanarity between the acetyl group and the thiazole ring.

An important general result is that the *X*-ray work validates the i.r. correlations shown in Table 2.

(*iii*) Earlier i.r. work [1] on a series of 5-trifluoroacetyl-2-(*N*,*N*-disubstituted amino)thiazoles showed that in solution all the

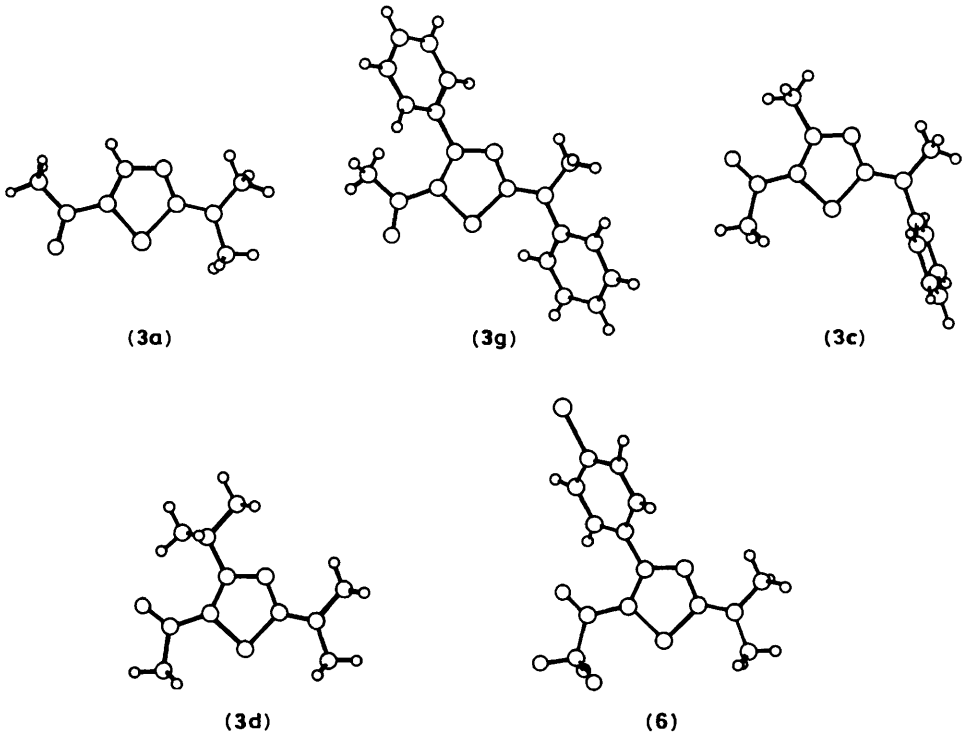
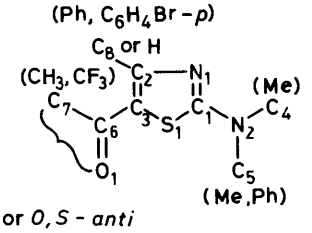


Figure. Structures of thiazoles from crystallographic results. (Table 3)

Table 3. Crystallographic results for compounds (**3a**,**c**,**d**, and **g**) and (**6**). 5-$CH_3(CF_3)$-CO conformations, bond lengths (Å), dihedral angles (°) between planes, C(2)–C(3)–C(6) angles (°), and perpendicular distances (Å) of N(2) from plane 3 (with standard deviations in parentheses)

Atomic Numbering



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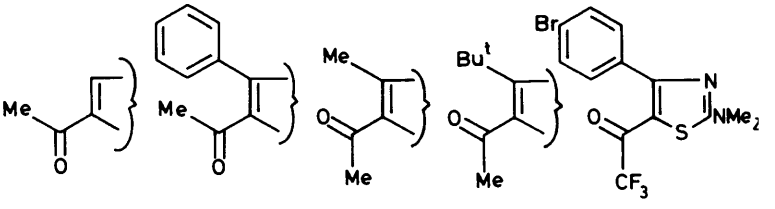

	(3a)	(3g)	(3c)	(3d)	(6)
$CH_3(CF_3)$–CO	*syn*	*syn*	*anti*	*anti*	*anti*
S(1)–C(1)	1.744(3)	1.732(2)	1.734(3)	1.720(2)	1.723(6)
C(1)–N(1)	1.321(4)	1.324(2)	1.319(3)	1.321(2)	1.330(8)
N(1)–C(2)	1.351(4)	1.368(2)	1.363(4)	1.364(2)	1.355(6)
C(2)–C(3)	1.358(4)	1.379(2)	1.370(4)	1.391(2)	1.389(7)
C(3)–S(1)	1.738(3)	1.742(2)	1.750(3)	1.748(2)	1.719(5)
C(1)–N(2)	1.342(4)	1.362(2)	1.351(3)	1.345(2)	1.328(7)
N(2)–C(4)	1.452(4)	1.463(2)	1.453(4)	1.448(2)	1.457(10)
N(2)–C(5)	1.449(5)	1.422(2)	1.441(4)	1.442(3)	1.457(9)
C(2)–C(8)	—	1.484(2)	1.495(4)	1.525(2)	1.477(8)
C(3)–C(6)	1.443(4)	1.464(3)	1.457(4)	1.458(2)	1.442(8)
C(6)–O(1)	1.225(4)	1.223(3)	1.222(4)	1.209(2)	1.211(8)
C(6)–C(7)	1.499(5)	1.503(3)	1.510(5)	1.511(3)	1.549(9)
Planes 1—2	175.0(4)	17.8(3)	1.1(3)	0.0(2)	167.5(5)
Planes 1—3	0.2(4)	8.9(2)	176.3(4)	0.3(2)	174.8(6)
Planes 1—4	—	45.1(2)	—	—	46.1(6)
Planes 1—5	—	41.8(3)	99.1(4)	—	—
Planes 3—5	—	37.8(3)	78.6(3)	—	—
C(2)–C(3)–C(6)	130.6(3)	134.9(2)	129.2(3)	133.6(2)	127.5(5)
N(2)–plane 3	0.022(4)	−0.026(3)	0.051(4)	0.49(3)	−0.046(6)

*Planes [and atoms contained]**
1 Thiazole [S(1)–C(1)–N(1)–C(2)–C(3)]
2 Carbonyl [C(3)–C(6)–C(7)–O(1)]
3 *Exo* N [C(1)–C(4)–C(5)–N(2)]
4 4-Aryl, (**3g**) and (**4**) [aromatic ring containing C(8)]
5 *N*-Phenyl, (**3c**) and (**3g**) [aromatic ring containing C(5)]

[a] Apart from N(2) all the atoms are within 0.02 Å of their planes.

Table 4. Bond lengths (Å)

	S(1)–C(1)	C(1)–N(1)	N(1)–C(2)	C(2)–C(3)	C(3)–S(1)
Average of compounds in Table 3:	1.731	1.323	1.360	1.377	1.739
Average of standard thiazoles:[a]	1.720	1.306	1.382	1.349	1.733

[a] Ref. 8.

Table 5. Crystallographic data for compounds (**3a,c,d**, and **g**) and (**6**)

Compound	(**3a**)	(**3g**)	(**3c**)	(**3d**)	(**6**)
Formula	$C_7H_{10}N_2OS$	$C_{18}H_{16}N_2OS$	$C_{13}H_{14}N_2OS$	$C_{11}H_{18}N_2OS$	$C_{13}H_{10}BrF_3N_2OS$
Rel. mol. mass	170.2	308.4	246.3	226.3	379.2
Crystal class	Monoclinic	Monoclinic	Orthorhombic	Orthorhombic	Orthorhombic
a/Å	11.699(4)	8.516(2)	10.365(2)	17.313(4)	8.408(1)
b/Å	5.675(3)	16.948(2)	9.990(1)	10.010(5)	11.061(2)
c/Å	13.112(4)	10.572(1)	12.347(2)	7.229(3)	15.896(2)
α/°	90	90	90	90	90
β/°	103.89(3)	91.42(2)	90	90	90
γ/°	90	90	90	90	90
U/Å^3	845.02	1 525.35	1 278.64	1 253.25	1 478.35
Space group	$P2_1/n$	$P2_1/c$	$Pna/2_1$	$Pnam$	$Pna/2_1$
Z	4	4	4	4	4
D_c/mg m^{-3}	1.388	1.343	1.280	1.200	1.704
$F(000)$	360	648	520	488	752
Crystal size/mm	0.1 × 0.55 × 0.75	0.5 × 0.55 × 0.75	0.5 × 0.75 × 0.525	0.5 × 0.85 × 0.65	0.38 × 0.33 × 0.22
Radiation	Cu-K_α	Cu-K_α	Cu-K_α	Mo-K_α	Cu-K_α
μ(cm^{-1})	29.7	18.5	19.3	2.34	57.8
$(\sin\theta/\lambda)_{max.}$	0.636	0.636	0.636	0.756	0.636
Total I[a]	2 834	4 491	3 686	3 645	2 934
Unique I[b]	1 429	2 892	1 363	1 755	1 410
R_m	0.051	0.024	0.035	0.015	0.028
n[c]	3	3	3	3	3
R	0.073	0.047	0.039	0.036	0.040
R_w	0.104	0.066	0.046	0.048	0.052
(Shift/error)^2[d]	21	110	39	0.03	7
$\Delta_{max.}$/eÅ^{-3}[e]	0.5	0.2	0.5	0.15	0.4
Weights	4 460, 6 310, 2 040, 185	12 960, 20 210, 9 154, 1 900	4 940, 7 670, 3 510, 771	245, 334, 99.9	662, 1 000, 492, 115

[a] Total number of reflections measured. [b] Number of unique reflections with intensity significantly above the background intensity. [c] Criterion for recognising observed reflections $I > n\sigma(I)$. [d] Ratio of least-squares shift to error in final refinement cycle. [e] Maximum height in final difference electron density synthesis.

compounds adopt a markedly predominant form which absorbs at higher wavenumber (*ca.* 1 675 cm^{-1}) than does the minor form (*ca.* 1 645 cm^{-1}), and which was tentatively assigned the *syn* structure. The present i.r. results with acetyl compounds suggest, however, that a higher wavenumber is characteristic of an *anti* form. One of the trifluoroacetyl derivatives studied previously [compound (**6**), Table 3] is now established by *X*-ray examination to be in the *anti* arrangement and this feature presumably applies throughout the series. The contrast in stereochemical preference between the similar pair of 4-aryl-5-acetyl and -trifluoroacetyl compounds (**3g**) and (**6**) is most simply attributed to the greater volume of a trifluoromethyl as compared with a methyl group; in the *syn* form of compound (**6**) there would be severe repulsion with the 4-aryl substituent.

(*iv*) As shown in Table 3, the *exo-N* atoms are only slightly displaced from the planes containing C(1), C(4), and C(5) (plane 3), and the angles between these planes and the thiazole ring (plane 1) are small. These features and the similarly small angles between planes 1 and 2 mentioned previously are such as to facilitate mesomeric interaction between the 2-NR_2 and 5-$CH_3(CF_3)CO$ groups. The contribution of dipolar forms has a significant influence on the bond lengths. Table 4 shows the comparison between the average bond lengths of the compounds studied here and the average values of 17 thiazoles (lacking such 2- and 5-substituents) for which well-determined crystallographic structures are available on request from the Cambridge Crystallographic Data Centre.* As expected, the mesomeric interaction leads to lengthening of the C(1)–N(1) and C(2)–C(3) bonds and shortening of the N(1)–C(2) bond; the effects (lengthening) with the S(1)–C(1) and C(3)–S(1) bonds are probably too small to be significant. These results and the low CO stretching values reinforce the conclusion[5] that 2-amino-5-carbonylthiazoles are to be regarded as extended amides rather than 6π-aromatic systems.

(*v*) In the 5-acetyl-2-(*N*-methyl-*N*-phenyl amino) compounds (**3c**) and (**3g**) (Figure) and a similar 5-carbaldehyde[5] the phenyl group is directed towards the sulphur atom. A possible explanation is as follows. The alternative arrangement would lead to repulsion between the phenyl group and the (necessarily) in-place lone pair of the *exo-N* atom. However, if, as suggested here, there is marked loss of aromaticity the sulphur's lone pairs will be disposed above and below plane 1, and involve a less severe interaction with the phenyl group.

Experimental

Preparative Work.—The thiazoles (**2a**—**e**)[5] and (**2f**)[6] were prepared by Hantzsch condensations as described earlier.[5]

* See Instructions for Authors (1981), para. 5.6.3. *J. Chem. Soc., Perkin Trans 1*, 1987, Issue 1.

Similarly phenacyl bromide and *N*-methyl-*N*-phenylthiourea gave 2-(N-*methylanilino*)-4-*phenylthiazole* (**2g**) (94%), m.p. 72—73 °C (from MeOH) (Found: C, 71.9; H, 5.5; N, 10.2. $C_{10}H_{14}N_2S$ requires C, 72.15; H, 5.3; N, 10.5%), δ 6.70 (1 H, s, 5-H).

Compounds (**1d**) *and* (**1g**).—A 1.56M solution of BuLi in hexane (4.51 ml) was added during 5 min to a solution of 2-dimethylamino-4-t-butylthiazole (**2d**) (1.21 g) in dry THF (tetrahydrofuran) (20 ml) which was stirred at −70 °C under dry N_2 during the addition, and then for a further 30 min. D_2O (0.5 ml)–THF (5 ml) was added, the cooling bath was removed, and after 30 min M Na_2CO_3 (40 ml) was added. Isolation with diethyl ether gave 5-deuterio-2-dimethylamino-4-t-butylthiazole (**1d**) (1.08 g), b.p. 102—103 °C/11 mmHg, *m/z* 185 (M^+, 50%) and 171 (100), no signal near δ 6 [*cf.* compound (**2d**), δ 6.04 (1 H, s, 5-H)]. Similarly 4-methyl-2-(*N*-methylanilino)thiazole (**2g**) gave the 5-deuterio derivative (**1g**) (83%), b.p. 164—166 °C/0.5 mmHg, *m/z* 205 (100%), no signal near δ 6.

Compounds (**3a**) *and* (**3d—g**).—A 1.56M solution of BuLi in hexane (15.6 ml) was added during 5 min to a solution of 2-dimethylaminothiazole (**2a**) (2.94 g) in dry THF (45 ml) which was stirred at −70 °C under dry N_2. After 30 min the solution was transferred during 10 min in a stream of N_2 *via* a metal cannula into a stirred solution of Ac_2O (freshly distilled; 5.1 g) in THF (25 ml) at −60 °C under N_2. The mixture was stirred at −60 °C for 30 min, the cooling bath was removed, and after a further 1 h M Na_2CO_3 (150 ml) was added. The material isolated with Et_2O was purified by flash chromatography on SiO_2 using CH_2Cl_2–EtOAc (1:1) to give 5-*acetyl*-2-*dimethylaminothiazole* (**3a**) (3.05 g), m.p. 101—103 °C (from C_6H_{12}) (Found: C, 49.4; H, 6.0; N, 16.6. $C_7H_{10}N_2OS$ requires C, 49.4; H, 5.9; N, 16.5%), *m/z* 170 (M^+, 90%), 155 (100), and 43 (38).

Similarly the thiazoles (**2d—g**) gave: 5-*acetyl*-2-*dimethylamino*-4-*t*-*butylthiazole* (**3d**) (77%), m.p. 151—152 °C (from C_6H_{14}) (Found: C, 58.1; H, 8.0; N, 12.3. $C_{11}H_{18}N_2OS$ requires C, 58.3; H, 8.0; N, 12.4%), *m/z* 226 (M^+, 50%), 211 (100), and 43 (40); 5-*acetyl*-2-(N-*methylanilino*)-4-*t*-*butylthiazole* (**3e**) (75%), m.p. 106—108 °C (from C_6H_{14}) (Found: C, 66.5; H, 6.9; N, 9.8. $C_{16}H_{20}N_2OS$ requires C, 66.6; H, 7.0; N, 9.7%), *m/z* 288 (90%), 273 (100), and 43 (45); 5-*acetyl*-2-*dimethylamino*-4-*phenylthiazole* (**3f**) (72%), m.p. 102—103 °C (from C_6H_{14}) (Found: C, 63.5; H, 5.8; N, 11.4. $C_{13}H_{14}N_2OS$ requires C, 63.4; H, 5.7; N, 11.4%), *m/z* 246 (M^+, 90%), 231 (100), and 43 (65); and 5-*acetyl*-2-(N-*methylanilino*)-4-*phenylthiazole* (**3g**) (74%), m.p. 154—155 °C (from MeOH) (Found: C, 70.3; H, 5.2; N, 9.1. $C_{18}H_{16}N_2OS$ requires C, 70.1; H, 5.2; N, 9.1%), *m/z* 308 (M^+, 100%), 293 (69), and 43 (43).

Compounds (**3b**) *and* (**3c**).—A solution of Br_2 (16.2 g) in CCl_4 (40 ml) was added during 1 h to a stirred dispersion of pentane-2,4-dione (10.1 g) in CCl_4 (60 ml)–H_2O (60 ml) at 0 °C. After 45 min the CCl_4 layer was separated, dried, and evaporated at 25 °C/16 mmHg to give an oil (15.6 g) shown by ^1H n.m.r. examination to be mainly (*ca.* 93%) 3-bromopentane-2,4-dione.

Table 6. Atomic co-ordinates for compound (**3a**)

Atom	*x/a*	*y/b*	*z/c*
S(1)	9 159.8(6)	2 460(1)	4 148.3(5)
C(1)	8 140(2)	716(5)	4 577(2)
C(2)	8 382(2)	−1 360(6)	3 246(2)
C(3)	9 130(2)	414(5)	3 156(2)
C(4)	6 894(3)	−156(7)	5 750(3)
C(5)	8 138(3)	3 508(7)	5 975(3)
C(6)	9 812(3)	806(6)	2 389(2)
C(7)	9 665(4)	−889(8)	1 490(3)
N(1)	7 815(2)	−1 226(5)	4 028(2)
N(2)	7 718(2)	1 372(5)	5 399(2)
O(1)	10 481(3)	2 489(5)	2 456(2)

Table 7. Atomic co-ordinates for compound (**3g**)

Atom	*x/a*	*y/b*	*z/c*
S(1)	1 804.3(6)	4 407.5(2)	4 968.4(4)
C(1)	2 167(2)	4 890(1)	6 390(2)
C(2)	3 040(2)	5 781(1)	5 045(2)
C(3)	2 617(2)	5 206(1)	4 178(2)
C(4)	1 882(3)	5 131(1)	8 621(2)
C(5)	1 231(2)	3 813(1)	7 736(2)
C(6)	1 817(2)	3 176(1)	7 081(2)
C(7)	1 267(3)	2 417(1)	7 318(2)
C(8)	162(3)	2 293(1)	8 228(2)
C(9)	−406(3)	2 925(1)	8 893(2)
C(10)	110(2)	3 687(1)	8 650(2)
C(11)	2 846(2)	5 090(1)	2 823(2)
C(12)	3 973(3)	5 595(1)	2 109(2)
C(13)	3 672(2)	6 577.1(9)	4 772(2)
C(14)	2 994(2)	7 039(1)	3 819(2)
C(15)	3 588(2)	7 781(1)	3 557(2)
C(16)	4 857(3)	8 069(1)	4 259(2)
C(17)	5 508(2)	7 623(1)	5 228(2)
C(18)	4 917(2)	6 881(1)	5 493(2)
O(1)	2 159(3)	4 550(1)	2 279(2)
N(1)	2 799(2)	5 600.3(8)	6 286(1)
N(2)	1 799(2)	4 591.6(9)	7 542(1)

Table 8. Atomic co-ordinates for compound (**3c**)

Atom	*x/a*	*y/b*	*z/c*
S(1)	10 058.2(6)	1 501.7(5)	7 412(3)
C(1)	8 834(3)	1 351(2)	6 245(4)
C(2)	8 888(3)	3 130(2)	6 408(4)
C(3)	9 850(3)	2 906(2)	7 307(5)
C(4)	7 382(4)	234(3)	4 922(5)
C(5)	8 998(3)	−586(2)	6 484(4)
C(6)	8 338(3)	−1 076(2)	7 511(5)
C(7)	8 857(4)	−1 990(3)	8 120(5)
C(8)	10 026(3)	−2 391(3)	7 707(4)
C(9)	10 693(3)	−1 885(3)	6 690(5)
C(10)	10 175(3)	−971(3)	6 065(4)
C(11)	10 638(3)	3 650(2)	8 090(4)
C(12)	11 634(3)	3 175(3)	9 023(4)
C(13)	8 436(3)	4 236(2)	6 024(4)
N(1)	8 313(2)	2 261(2)	5 814(4)
N(2)	8 459(2)	355(2)	5 842(4)
O(1)	10 512(3)	4 632(2)	8 001(4)

Table 9. Atomic co-ordinates for compound (**3d**)

Atom	*x/a*	*y/b*	*z/c*
S(1)	4 829	1 052	2 500
O(1)	5 443	−2 689	2 500
N(1)	6 298	1 453	2 500
N(2)	5 554	3 416	2 500
C(1)	5 626	2 078	2 500
C(2)	6 205	100	2 500
C(3)	5 442	−336	2 500
C(4)	4 793	4 016	2 500
C(5)	6 233	4 252	2 500
C(6)	5 083	−1 654	2 500
C(7)	4 211	−1 716	2 500
C(8)	6 940	−739	2 500
C(9)	7 653	165	2 500
C(10)	6 971	−1 609	4 245

Table 10. Atomic co-ordinates for compound (**6**)

Atom	*x/a*	*y/b*	*z/c*
BR(1)	234(1)	3 527.4(7)	4 550(6)
C(1)	3 456(6)	4 161(4)	11 455(8)
C(2)	2 643(6)	3 489(3)	9 818(7)
C(3)	2 858(7)	2 793(3)	10 560(8)
C(4)	4 372(10)	4 683(5)	13 393(9)
C(5)	3 997(9)	5 652(4)	11 653(9)
C(6)	2 418(7)	1 934(4)	10 304(8)
C(7)	2 986(7)	1 252(4)	11 207(8)
C(8)	2 086(6)	3 484(3)	8 552(7)
C(9)	946(8)	4 055(4)	8 189(8)
C(10)	388(8)	4 072(4)	7 018(9)
C(11)	1 024(8)	3 513(4)	6 193(8)
C(12)	2 171(9)	2 953(4)	6 510(8)
C(13)	2 712(7)	2 937(4)	7 705(8)
S(1)	3 548(2)	3 131.9(9)	11 939(6)
N(1)	2 991(5)	4 247(3)	10 313(7)
N(2)	3 852(6)	4 808(3)	12 152(8)
F(1)	2 499(6)	1 409(3)	12 335(7)
F(2)	4 527(5)	1 206(4)	11 292(9)
F(3)	2 357(7)	520(2)	10 957(7)
O(1)	1 686(6)	1 687(3)	9 430(7)

A solution of this oil (4.62 g) and *N,N*-dimethylthiourea (2.52 g) in Me_2CO (40 ml) was boiled under reflux for 30 min, cooled, and basified with M Na_2CO_3 (100 ml). The material isolated with EtOAc was sublimed at 140—142 °C/0.03 mmHg and then crystallised from dry Et_2O to give *5-acetyl-2-dimethylamino-4-methylthiazole* (**3b**) (2.48 g), m.p. 69—70 °C (Found: C, 52.1; H, 6.5; N, 15.0. $C_8H_{12}N_2OS$ requires C, 52.1; H, 6.6; N, 15.2%), *m/z* 184 (M^+, 82%), 169 (100), and 43 (39). Similarly 3-bromopentane-2,4-dione and *N*-methyl-*N*-phenylthiourea gave *5-acetyl-4-methyl-2-(N-methylanilino)thiazole* (**3c**) (79%), m.p. 92—93 °C (from Pr^iOH) (Found: C, 63.3; H, 5.65; N, 11.2. $C_{13}H_{14}N_2OS$ requires C, 63.4; H, 5.7; N, 11.4%), *m/z* 246 (100%), 231 (90), and 43 (41).

Crystallographic Work.—The determinations were carried out as described in ref. 5. The results, presented in standard form, are given in Tables 5—10.

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