13. *Studies of Heterocyclic Compounds. Part I. A Synthesis of 6-Substituted Pyrrolo[2,1-b]thiazoles.*

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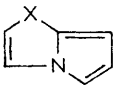
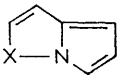
3-Acetonyl- and 3-phenacyl-2-alkylthiazolium salts are cyclised by sodium acetate in aprotic solvents. In acetic anhydride pyrrolo[2,1-*b*]thiazoles, or, more usually, their mono- and di-acetyl derivatives, are obtained in high yield. Deacetylation is readily carried out with acid. In dimethylformamide pyrrolo[2,1-*b*]thiazoles are produced directly in low yield.

We shall describe in this and succeeding Papers studies of the chemistry of the pyrrolo-[2,1-*b*]azoles (I) and pyrrolo[1,2-*b*]azoles (II), derived from indolizine by replacement of the 7,8- or 5,6-bond, respectively, by a heteroatom in Group V or VI of the Periodic Table. These heterocycles are isoelectronic with indolizine and other bicyclic 10π-electron structures, one pair of non-bonding electrons from each heteroatom being formally available for overlap.

(I)   (II) X = O, S, or NH, etc.

At the beginning of our work the preparation of one simple derivative in each case of pyrrolo[2,1-*b*]thiazole (I; X = S) and pyrrolo[2,1-*b*]imidazole (I; X = NH) constituted the known chemistry of these heterocycles. This Paper describes a general synthesis of 6-alkyl- and 6-aryl-pyrrolo[2,1-*b*]thiazoles from thiazoles.

3-Methyl-6-phenylpyrrolo[2,1-*b*]thiazole (VIIg), the first compound of this series to be reported,[1] had been prepared by quaternisation of 2,4-dimethylthiazole with phenacyl bromide, followed by cyclisation of the resulting 2,4-dimethyl-3-phenacylthiazolium bromide (IIIa) with aqueous sodium carbonate. This reaction is based on the flexible Chichibabin synthesis of indolizines. With the intention of exploiting the method we re-examined the preparation of the base (VIIg), and also cyclised 2-methyl-3-phenacylbenzothiazolium bromide (IV) with aqueous sodium hydrogen carbonate. Yields were low in both reactions. We also attempted to prepare simpler derivatives of pyrrolo-[2,1-*b*]thiazole, and selected for preliminary examination the cyclisation of 2-methyl-3-phenacylthiazolium bromide (Va) and 3-acetonyl-2-methylthiazolium bromide (Vb). The former, on treatment with aqueous sodium hydroxide, carbonate, hydrogen carbonate, or acetate, gave a polymer of low molecular weight containing only traces of 6-phenylpyrrolo[2,1-*b*]thiazole (VIIIa).* Cyclisation of the salt (Vb) by the same reagents, with isolation of the product by steam-distillation, gave only traces of 6-methylpyrrolo[2,1-*b*]-thiazole (VIa).

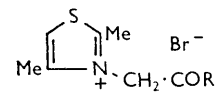
Quaternisation of 2,4-dimethylthiazole with bromobiacetyl or ethyl bromopyruvate and cyclisation of the products (IIIb and c) was next carried out. The object of this was, first, to increase the electrophilic reactivity of the keto-group in compound (III) for cyclisation by flanking it with acetyl and ethoxycarbonyl groups, and secondly, to obtain the acid (VIIe) directly, or by degradation of the ketone (VIId), for decarboxylation to the base (VIIf). This reaction sequence would constitute a synthesis of pyrrolo[2,1-*b*]thiazoles free from substituents in the pyrrole ring. The salts (IIIb and c) could not be crystallised or converted into solid derivatives, and their aqueous extracts were cyclised directly with sodium hydrogen carbonate. 6-Acetyl-3-methylpyrrolo[2,1-*b*]thiazole (VIId) was obtained in 12% yield. A very small quantity of acidic material was isolated from the bromide

* Pyrrolo[2,1-*b*]thiazoles are readily detected at low concentration with Ehrlich's reagent.

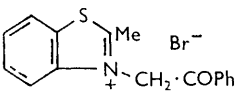
[1] Kondo and Nagasawa, *J. Pharm. Soc. Japan*, 1937, **57**, 1050.

(IIIc), but methylation followed by gas–liquid chromatography showed it to be inhomogeneous. Aqueous base thus appeared to be unsuitable for cyclisation of the quaternary thiazolium salts. At this stage we found that cyclisation could be effected under aprotic conditions by boiling the quaternary salt with two equivalents of sodium acetate in acetic anhydride. The resulting pyrrolo[2,1-*b*]thiazoles are acetylated *in situ*, but the acetyl groups are readily removed by acid hydrolysis later. We have applied this procedure to the preparation of the pyrrolo[2,1-*b*]thiazoles (VIa—d), (VIIa—c), (VIIIa—c), (IXa and b), and (X).

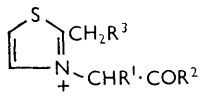
Several conclusions were drawn from an examination of the composition of the cyclisation products. First, the yields in the cyclisation step are almost quantitative. Secondly, the extent of acetylation depends on the degree and position of substitution of the pyrrolo-[2,1-*b*]thiazole. Thus 5,6- (VIb) and 6,7-dimethylpyrrolo[2,1-*b*]thiazole (VIc) were obtained as monoacetyl derivatives, while cyclisation of the bromide (Vb) gave a mixture of a mono- and a di-acetyl-6-methylpyrrolo[2,1-*b*]thiazole. In no case was a tri- or tetra-



(III) a: R = Ph
b: R = Ac
c: R = CO_2Et

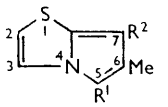


(IV)

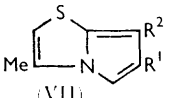


(V)

	R¹	R²	R³
a:	H	Ph	H
b:	H	Me	H
c:	Me	Me	Me

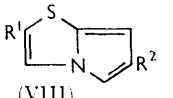


(VI) a: R¹ = R² = H
b: R¹ = Me, R² = H
c: R¹ = H, R² = Me
d: R¹ = R² = Me



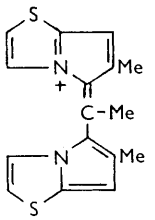
(VII)

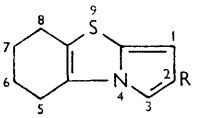
	R¹	R²		R¹	R²
a:	Me	H	e:	CO_2H	H
b:	Me	Me	f:	H	H
c:	Me	Ph	g:	Ph	H
d:	Ac	H			



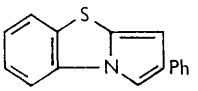
(VIII)

	R¹	R²
a:	H	Ph
b:	Me	Me
c:	Me	Ph





(IX) a: R = Me. b: R = Ph



(X)

(XI)

acetyl derivative detected. Exceptionally, cyclisation of the salt (Vc) gave 5,6,7-trimethylpyrrolo[2,1-*b*]thiazole (VId) alone. These results indicate that the acetyl groups occupy the 5- and/or the 7-position. Confirmation of this will be discussed in a later Paper. Thirdly, the nature of the anion influences the composition of the cyclisation product. 3-Acetonyl-2-methylthiazolium perchlorate (Vb; ClO_4 for Br) afforded a product containing a higher percentage of diacetyl-6-methylpyrrolo[2,1-*b*]thiazole than was obtained from the corresponding bromide (Vb). This probably results because perchloric acid is a stronger acid than hydrobromic acid and hence a more effective acetylation catalyst.

The deacetylation stage is critical because of the possibility of condensation of the acetyl compound with the pyrrolo[2,1-*b*]thiazole during hydrolysis, which would lead to cyanine dyes, *e.g.*, the cation (XI) from 6-methylpyrrolo[2,1-*b*]thiazole (VIa) and its 5-acetyl derivative. Dilute or concentrated hydrochloric acid was used for deacetylation, with the addition of dioxan or acetic acid where necessary to facilitate dissolution. High acid concentrations promote the formation of cyanine dyes, and the yields of pyrrolo[2,1-*b*]-thiazoles were lower from diacetyl or acetylated phenyl derivatives which require high acid concentrations for deacetylation.

We also examined other systems of bases in aprotic solvents for the cyclisation of

3-acetonyl- and 3-phenacyl-2-alkylthiazolium salts. The results, summarised in Table 2 (Experimental section), showed that alkali-metal acetates in dimethylformamide alone are effective in giving pyrrolo[2,1-*b*]thiazoles, but in poor yield.

Quaternisation of thiazoles with phenacyl bromide proceeds smoothly in boiling ethanol. 3-Acetonylthiazolium salts are best prepared in chloroform, either for a short period at the boiling point or for a prolonged period at room temperature. In some cases it was expedient to allow the thiazole to react with bromoacetone or 3-bromobutan-2-one in the absence of solvent.

Hitherto, ethyl bromopyruvate has been used little, and bromobiacetyl not at all, in quaternisations. In trial reactions with 2,4-dimethylthiazole neither gave a solid bromide, perchlorate, or picrate in the common solvents under a variety of conditions, and the residue after removal of solvent was utilised in further reactions. Violent exothermic reactions and much decomposition took place in the absence of a solvent. In ether, almost quantitative precipitation of 2,4-dimethylthiazolium bromide occurred. Stoicheiometric considerations suggest that carbene intermediates (:CH·CO·CO_2Et and :CH·CO·COMe) may be the other products of these reactions.

Experimental

Melting points were determined on a Kofler hot-stage apparatus. Gas–liquid chromatography was on a Pye Argon instrument.

Materials.—Acetonitrile was purified by boiling it for 1 hr. over phosphoric anhydride, then distilled, and it was redistilled before use. Chloroform was boiled over phosphoric anhydride and distilled; it was passed through a dry-packed column of alumina before use. Perchloric acid refers to 70—72% w/w perchloric acid of AnalaR grade, unless otherwise specified.

Quaternisation of Thiazoles with (A) *Bromoacetone and* (B) *Phenacyl Bromide.*—These were by one of the following procedures (for details see Table 1).

Procedure A1. A solution of the thiazole (0·1 mole) and bromoacetone (13·7 g., 0·1 mole) in chloroform was left at room temperature. The oil which had separated crystallised, and the pale yellow solid was recrystallised from ethanol. In cases where the bromide obtained by procedures A1 and A2 could not be recrystallised satisfactorily a sample was converted into the perchlorate for characterisation as follows. A 10% excess of perchloric acid was added to a cold solution of the bromide in ethanol (20 ml./g.). The perchlorate was filtered off, washed with ether, and recrystallised from ethanol unless otherwise stated.

Procedure A2. A solution of the thiazole (0·1 mole) and bromoacetone (13·7 g., 0·1 mole) in chloroform was boiled, cooled, and thereafter worked up as described in the foregoing procedure.

Procedure A3. A solution of the thiazole (0·1 mole) and bromoacetone (13·7 g., 0·1 mole) in chloroform was boiled. Ethanol (30 ml.) and then perchloric acid (10 ml., 0·1 mole) were added. The perchlorate was washed with ether and recrystallised from ethanol.

Procedure A4. A mixture of the thiazole (0·1 mole) and bromoacetone (13·7 g., 0·1 mole) was heated at 70°. Cooling and trituration of the resulting brown gum with acetone gave the bromide which was washed with ether, and converted into the perchlorate as described in procedure A1.

Procedure B. A solution of the thiazole (0·1 mole) and phenacyl bromide (19·9 g., 0·1 mole) in dry ethanol was boiled. The bromide which crystallised was filtered from the cooled solution, washed with ether, and recrystallised from ethanol.

Pyrrolo[2,1-b]*thiazoles from* 3-*Acetonyl- and* 3-*Phenacyl-thiazolium Salts.*—The salts were cyclised by the following procedure. (Minor deviations from this procedure are given in appropriate cases.) A mixture of the bromide, fused sodium acetate (164 mg., 2 mmoles per mmole of salt), and acetic anhydride (10 ml. per g. of salt) was boiled for 2 hr., cooled, and poured into water (20 ml. per mmole of salt). The resulting mixture was kept at room temperature for 12 hr. before being extracted with chloroform. The chloroform extracts were washed successively with water, dilute potassium carbonate solution, and water, and dried (Na_2SO_4). Evaporation of the solution gave the crude acetylated pyrrolo[2,1-*b*]thiazole.

Deacetylation conditions are critical and are given individually. In the preparation of alkyl pyrrolo[2,1-*b*]thiazoles the mixture, after deacetylation, was made alkaline with solid

TABLE 1.

Quaternisation of thiazoles with (A) bromoacetone and (B) phenacyl bromide.

Procedure, solvent (ml.)	Thiazole	Reaction time (hr.)	Thiazolium salt	Product no.	Yield (%)
A[1] 10	2-Me	72	3-Acetonyl-2-Me, bromide	1a	89
			3-Acetonyl-2-Me, perchlorate	1b	92
B[b] 100	,,	12	2-Me-3-phenacyl, bromide	2	89
A[1][c] 10	2,4-Me_2	60	3-Acetonyl-2,4-Me_2, bromide	3	81
A2 16	2,5-Me_2	4	3-Acetonyl-2,5-Me_2, bromide	4a	90
			3-Acetonyl-2,5-Me_2, perchlorate	4b	93
B 60	,,	10	2,5-Me_2-3-phenacyl, bromide	5	85
A2[e] 10	2-Et	6	3-Acetonyl-2-Et, bromide	6a	64
			3-Acetonyl-2-Et, perchlorate	6b	94
A2[f] 13	2-Et-4-Me	12	3-Acetonyl-2-Et-4-Me, bromide	7a	86
			3-Acetonyl-2-Et-4-Me, picrate[g,h]	7b	88
B[b] 50	4,5,6,7-H_4-2-Me-benzo	12	4,5,6,7-H_4-2-Me-3-phenacyl, bromide	8	82
A3 15	4,5,6,7-H_4-2-Me-benzo	12	3-Acetonyl-4,5,6,7-H_4-2-methylbenzo, perchlorate	9	52
A4	2-Benzyl-4-Me	8	3-Acetonyl-2-benzyl-4-Me, bromide	10a	85
			3-Acetonyl-2-benzyl-4Me, perchlorate	10b	95
B[k] 40	2-Me-benzo	21	2-Me-3-phenacylbenzo, bromide[l]	11	54

No.	Form	M. p.	Found N (%)	Formula	Required N (%)
1a	Pale yellow crystals *	>200°[a]	—	—	—
1b	Colourless needles	124—126	5·5	$C_7H_{10}ClNO_5S$	5·6
2	Colourless cubes	204—205·5	—	$C_{12}H_{12}BrNOS$[o]	—
3	Colourless cubes	208—211 †	5·8	$C_8H_{12}BrNOS$[p]	5·6
4a	Yellow cubes *	172—174	—	—	—
4b	Colourless needles	156·5—158	5·1	$C_8H_{12}ClNO_5S$	5·2
5	Colourless needles	212—212·5[d]	4·3	$C_{13}H_{14}BrNOS$	4·5
6a	Colourless crystals ‡	§	—	—	—
6b	Colourless needles	139—141	5·3	$C_8H_{12}ClNO_5S$	5·2
7a	Brown amorphous solid	142—145 †	—	—	—
7b	Yellow needles	161—163[i]	13·7	$C_{15}H_{16}N_4O_8S$	13·6
8	Colourless prisms[j]	204—206 †	3·9	$C_{16}H_{18}BrNOS$	4·0
9	Colourless prisms	130—132	4·4	$C_{11}H_{16}ClNO_5S$	4·5
10a	Yellow prisms *	165—168 †	—	—	—
10b	Colourless plates	159—161	3·9	$C_{14}H_{16}ClNO_5S$	4·1
11	Colourless prisms[m]	233·5—235·5[n]	—	—	—

* Recrystallisation unsatisfactory. † With decomp. ‡ Hygroscopic; could not be recrystallised. § Hygroscopic; m. p. could not be determined.

[a] Decomp. without melting. [b] Reaction solution diluted with ether (100 ml.). [c] Ether (25 ml.) added after product had crystallised; solution left for 2 hr. [d] Darkens >205°. [e] Acetone (60 ml.) added to initiate crystallisation. [f] Reaction solution diluted with ethyl acetate (40 ml.). [g] Perchlorate failed to crystallise. [h] Prepared by mixing saturated boiling ethanolic solutions containing equimolecular quantities of the bromide and picric acid. [i] Softens >150°. [j] Recryst. from acetonitrile. [k] Chloroform as solvent. [l] The salt which had precipitated after 6 hr. was filtered off and washed with ether, and the combined filtrates were concentrated to 50 ml. before boiling was continued. [m] Recryst. from acetone–methanol (1 : 1). [n] Lit.,[2] 228—229°. [o] Found: Br, 26·4. Reqd.: Br, 26·8%. [p] Found: S, 12·7. Reqd.: S, 12·8%.

sodium hydroxide and steam-distilled. The distillate was extracted with ether, and the ether extracts were washed successively with water, potassium carbonate solution, and water, and dried (K_2SO_3) before evaporation. Phenyl- and benzo-pyrrolo[2,1-*b*]thiazoles were extracted directly with ether or chloroform, after deacetylation and subsequent dilution with much water. The extracts were washed successively with water, sodium carbonate solution, and water, and dried (K_2CO_3) before evaporation.

Percentage yields of the pyrrolo[2,1-*b*]thiazoles are based on the thiazolium salts. Distillation and sublimation temperatures are those of the heating block.

Charge-transfer complexes of the pyrrolo[2,1-*b*]thiazoles with 1,3,5-trinitrobenzene were

[2] Kröhnke and Friedrich, *Chem. Ber.*, 1963, **96**, 1195.

prepared by addition of the base (0·5 mmole) in cold ethanol (2 ml.) to a boiling saturated solution of the reagent (107 mg., 0·5 mmole) in ethanol. Recrystallisation was from ethanol.

Pyrrolo[2,1-*b*]thiazolium picrates * were prepared by addition of a boiling saturated solution of picric acid (115 mg., 0·5 mmole) in ethanol to the pyrrolo[2,1-*b*]thiazole (0·5 mmole) in cold ethanol (1 ml.). Recrystallisation was from ethanol.

6-*Methylpyrrolo*[2,1-b]*thiazole*. Cyclisation of 3-acetonyl-2-methylthiazolium bromide (11·8 g., 50 mmoles) and extraction with methylene chloride gave the acetylated 6-methylpyrrolo-[2,1-*b*]thiazole as an oil (3·67 g.) which slowly solidified. This was boiled for 3 hr. with concentrated hydrochloric acid (18 ml.) and water (60 ml.). The product sublimed at 90—95°/10 mm. and afforded 6-*methylpyrrolo*[2,1-b]*thiazole* (VIa) (1·5 g., 68%) as colourless needles, m. p. 57—58°, which rapidly become violet and then black in air. The *trinitrobenzene complex* formed crimson needles (79%), m. p. 122·5—124° (Found: N, 16·4. $C_{13}H_{10}N_4O_6S$ requires N, 16·0%). 6-*Methyl*-5H-*pyrrolo*[2,1-b]*thiazolium picrate* was obtained as yellow needles (97%), m. p. 155—160° (decomp.) (Found: C, 42·6; H, 3·0. $C_{13}H_{10}N_4O_7S$ requires C, 42·6; H, 2·8%).

6-*Phenylpyrrolo*[2,1-b]*thiazole*. Cyclisation of 2-methyl-3-phenacylthiazolium bromide (14·9 g., 50 mmoles) (4 hr., reflux) gave acetylated 6-phenylpyrrolo[2,1-*b*]thiazole as a viscous yellow oil (9·3 g.). This was boiled for 3 hr. with concentrated hydrochloric acid (80 ml.). Dilution with water (1·5 l.) and four extractions with ether yielded a tarry residue which distilled at 125—130°/0·1 mm. 6-*Phenylpyrrolo*[2,1-*b*]thiazole (VIIIa) was obtained as a colourless sublimate (1·94 g., 20%) which crystallised from acetone as colourless needles, m. p. 200—202° (Found: C, 72·4; H, 4·6; N, 7·1; S, 16·1. $C_{12}H_9NS$ requires C, 72·3; H, 4·6; N, 7·0; S, 16·1%).

3,6-*Dimethylpyrrolo*[2,1-b]*thiazole*. Cyclisation of 3-acetonyl-2,4-dimethylthiazolium bromide (12·5 g., 50 mmoles) gave acetylated 3,6-dimethylpyrrolo[2,1-*b*]thiazole as a tarry solid (10·7 g.). A portion (3·6 g.) was boiled for 3 hr. with concentrated hydrochloric acid (20 ml.) and water (60 ml.). The product on being distilled at 105—110°/10 mm. afforded 3,6-*dimethylpyrrolo*-[2,1-b]*thiazole* (VIIa) (1·56 g., 62%) as a colourless oil which rapidly became brown and then black in air. The *trinitrobenzene complex* formed deep red needles (82%), m. p. 123—125° (softens >115°) (Found: N, 15·2. $C_{14}H_{12}N_4O_6S$ requires N, 15·4%).

2,6-*Dimethylpyrrolo*[2,1-b]*thiazole*. Crude acetylated 2,6-dimethylpyrrolo[2,1-*b*]thiazole was obtained as a brown solid (10·5 g.) from 3-acetonyl-2,5-dimethylthiazolium bromide (12·5 g., 50 mmoles). A portion (2·1 g.) was boiled for 4 hr. with concentrated hydrochloric acid (7 ml.) and water (30 ml.). Distillation of the product at 105—110°/10 mm. afforded 2,6-*dimethyl-pyrrolo*[2,1-b]*thiazole* (VIIIb) (990 mg., 65%) as colourless plates, m. p. 80—81° (sublimation >75°) which rapidly became brown and then black in air. The *trinitrobenzene complex* was obtained as bright red needles (80%), m. p. 125·5—128° (decomp.) (softens >121°) (Found: N, 15·0. $C_{14}H_{12}N_4O_6S$ requires N, 15·4%).

2-*Methyl*-6-*phenylpyrrolo*[2,1-b]*thiazole*. Cyclisation of 2,5-dimethyl-3-phenacylthiazolium bromide (31·2 g., 0·1 mole) gave the acetylated base as a viscous oil (26·7 g.) which slowly solidified. This was boiled for 6 hr. with dioxan (160 ml.), water (100 ml.), and concentrated hydrochloric acid (20 ml.). Dilution with water (2 l.) and extraction with chloroform gave a green oil which was distilled at 140—150°/0·1 mm. 2-*Methyl*-6-*phenylpyrrolo*[2,1-b]*thiazole* (VIIIc) (7·65 g., 36%), sublimed and after recrystallisation from ethanol, formed colourless plates, m. p. 200—203° (decomp.) (sublimation >150°) (Found: C, 73·0; H, 5·4; N, 6·7; S, 15·3. $C_{13}H_{11}NS$ requires C, 73·2; H, 5·2; N, 6·6; S, 15·0%).

6,7-*Dimethylpyrrolo*[2,1-b]*thiazole*. Cyclisation of 3-acetonyl-2-ethylthiazolium bromide (5 g., 20 mmoles) gave the crude acetylated base as green crystals (3·83 g.). A portion (1·28 g.) was boiled for 2 hr. with concentrated hydrochloric acid (5 ml.), acetic acid (10 ml.), and water (10 ml.). The product distilled at 105—110°/10 mm., giving 6,7-*dimethylpyrrolo*[2,1-b]*thiazole* (VIc) (890 mg., 89%) as a colourless oil which rapidly became blue and then black in air. The *trinitrobenzene complex* formed brown needles (82%) which decomposed slowly to a black liquid >135° (Found: N, 15·1. $C_{14}H_{12}N_4O_6S$ requires N, 15·4%).

3,6,7-*Trimethylpyrrolo*[2,1-b]*thiazole*. Ring-closure of 3-acetonyl-2- ethyl-4-methylthiazolium, bromide (13·2 g., 0·05 mole) gave the acetylated base as an oil (10·4 g.) which slowly solidified. A portion (1·04 g.) was boiled for 2 hr. with concentrated hydrochloric acid (5 ml.) and acetic acid (10 ml.). Distillation of the product at 115—120°/10 mm. gave 3,6,7-*trimethylpyrrolo*-[2,1-b]*thiazole* (VIIIb) (810 mg., 98%) as colourless needles, m. p. 44—45°, which rapidly became

* In a forthcoming publication on the nuclear magnetic resonance spectra of pyrrolo[2,1-*b*]thiazolium salts it will be shown that protonation of pyrrolo[2,1-*b*]thiazoles occurs preferentially at C-5.

green and then black in air. The *trinitrobenzene* complex formed brown needles (89%) which decomposed slowly to a black liquid >130° (Found: N, 15·1. $C_{15}H_{14}N_4O_6S$ requires N, 14·8%).

5,6,7,8-*Tetrahydro*-2-*phenylpyrrolo*[2,1-b]*benzothiazole.* Cyclisation of 4,5,6,7-tetrahydro-2-methyl-3-phenacylbenzothiazolium bromide (17·6 g., 50 mmoles) gave the acetylated base (12·03 g.) as a semicrystalline paste. This was boiled for 4 hr. with concentrated hydrochloric acid (60 ml.), acetic acid (120 ml.), and water (120 ml.). Dilution with water (2 l.) and extraction with chloroform gave a residue which was sublimed at 165—170°/0·1 mm. 5,6,7,8-*Tetrahydro*) 2-*phenylpyrrolo*[2,1-b]*benzothiazole* (IXb) was obtained as a colourless sublimate (7·8 g., 62%). Recrystallisation from ethanol gave colourless plates, m. p. 108—109° (Found: C, 75·7; H, 6·0; N, 5·7; S, 13·2. $C_{16}H_{15}NS$ requires C, 75·9; H, 6·0; N, 5·5; S, 12·7%).

5,6,7,8-*Tetrahydro*-2-*methylpyrrolo*[2,1-b]*benzothiazole.* The acetylated base (8·45 g.) from the cyclisation of 3-acetonyl-4,5,6,7-tetrahydro-2-methylbenzothiazolium perchlorate (9·3 g., 30 mmoles) was boiled for 4 hr. with concentrated hydrochloric acid (43 ml.), acetic acid (85 ml.), and water (85 ml.). Distillation of the oily product at 160—165°/10 mm. afforded 5,6,7,8-*tetrahydro*-2-*methylpyrrolo*[2,1-b]*benzothiazole* (IXa) (4·3 g., 75%) as colourless prisms, m. p. 55·5—56·5°, which rapidly became brown in air. The *trinitrobenzene complex* formed deep red needles (84%), m. p. 121—122° (Found: N, 13·8. $C_{17}H_{16}N_4O_6S$ requires N, 13·9%).

3,6-*Dimethyl*-7-*phenylpyrrolo*[2,1-b]*thiazole.* Cyclisation of 3-acetonyl-2-benzyl-4-methylthiazolium perchlorate (9·78 g., 30 mmoles) and extraction with methylene chloride gave the acetylated base (7·77 g.) as a tarry paste. This was boiled for 5 hr. with concentrated hydrochloric acid (40 ml.), acetic acid (80 ml.), and water (80 ml.). Dilution with water (2 l.) and extraction with chloroform gave an oil which was distilled at 140°/0·1 mm. 3,6-*Dimethyl*-7-*phenylpyrrolo*[2,1-b]*thiazole* (VIIc) was obtained as a colourless oil (435 mg., 6·4%).

2-*Phenylpyrrolo*[2,1-b]*benzothiazole.* Cyclisation of 2-methyl-3-phenacylbenzothiazolium bromide (34·8 g., 0·1 mole) (4 hr., reflux) gave the acetylated base as a brown oil (30 g.). A portion (3 g.) was boiled for 3 hr. with concentrated hydrochloric acid (10 ml.) and acetic acid (10 ml.). Dilution of the dark red solution with water (300 ml.) and extraction with ether gave an oil which was distilled at 150—155°/0·1 mm. 2-Phenylpyrrolo[2,1-*b*]benzothiazole (X) sublimed as pale yellow crystals (1·03 g., 41%). Recrystallisation from ethanol gave colourless needles, m. p. 124—125° (lit.,[2] 127—129°) (Found: C, 77·2; H, 4·5; N, 5·5; S, 12·6. Calc. for $C_{16}H_{11}NS$: C, 77·1; H, 4·5; N, 5·6; S, 12·9%).

Preparation of 5,6-*Dimethylpyrrolo*[2,1-b]*thiazole.*—A mixture of 2-methylthiazole (5·94 g., 60 mmoles) and 3-bromobutan-2-one (9 g., 60 mmoles) was heated at 50° for 22 hr. Sodium acetate (9·84 g., 120 mmoles) and acetic anhydride (150 ml.) were added, and the mixture was boiled for 2 hr., cooled, and poured into water (1 l.). After 12 hr. at room temperature the mixture was extracted with chloroform. The extracts were washed successively with water, potassium carbonate solution, and water, and dried (Na_2SO_4). Evaporation gave the acetylated base (10·93 g.) as a green oil which partly solidified to a tarry paste.

A portion (2·2 g.) was boiled for 2 hr. with concentrated hydrochloric acid (11 ml.), acetic acid (25 ml.), and water (25 ml.). The cooled solution was diluted with water (150 ml.), made alkaline by the addition of solid sodium hydroxide, and steam-distilled. The distillate was extracted with ether, and the ether extracts were washed with 0·25M-sulphuric acid (2 × 200 ml.) and water, dried (K_2SO_3), and evaporated. Distillation of the residual oil at 110—115°/10 mm afforded 5,6-*dimethylpyrrolo*[2,1-b]*thiazole* (VIb) (540 mg., 30% from 2-methylthiazole) as a pale yellow oil which darkened in air. The *trinitrobenzene complex* formed brown needles (77%), m. p. 124—127° (decomp.) (Found: C, 45·8; H, 3·2; N, 15·4; S, 8·9. $C_{14}H_{12}N_4O_6S$ requires C, 46·1; H, 3·3; N, 15·4; S, 8·8%). Reaction with picric acid gave yellow needles (80%), m. p. 105—113° (decomp.), which consisted of a mixture of 5,6-dimethyl-5*H*- and -7*H*-pyrrolo-[2,1-*b*]thiazolium picrate (Found: C, 43·7; H, 3·1; N, 14·5. Calc. for $C_{14}H_{12}N_4O_7S$: C, 44·2; H, 3·2; N, 14·7%).

Preparation of 5,6,7-*Trimethylpyrrolo*[2,1-b]*thiazole.*—A solution of 2-ethylthiazole (5·65 g., 50 mmoles) and 3-bromobutan-2-one (7·55 g., 50 mmoles) in chloroform (5 ml.) was boiled for 7 hr. Ethyl acetate (50 ml.) was added to the cooled mixture, and the precipitated 2-ethyl-3-(1-methyl-2-oxopropyl)thiazolium bromide (11·3 g., 86%) was filtered off, washed with ethyl acetate, and dried at once *in vacuo*. The salt is very hygroscopic and its m. p. could not be determined.

A mixture of the bromide (5·28 g., 20 mmoles), sodium acetate (3·28 g., 40 mmoles), and

acetic anhydride (50 ml.) was boiled for 2 hr. The cooled mixture was diluted with water (150 ml.), made alkaline with solid sodium hydroxide, and steam-distilled. The distillate was extracted with ether, and the ether extract was dried (K_2CO_3) before removal of the solvent. Distillation of the residual oil at 130—135°/10 mm. gave 5,6,7-*trimethylpyrrolo*[2,1-b]*thiazole* (VId) (1·99 g., 60% from the bromide) as a pale yellow oil. The *trinitrobenzene complex* formed dark brown needles (93%), m. p. 149—152° (decomp.) (Found: N, 14·9. $C_{15}H_{14}N_4O_6S$ requires N, 14·8%). 5,6,7-*Trimethyl*-5H-*pyrrolo*[2,1-b]*thiazolium picrate* was obtained as yellow prisms (64%), m. p. 130—133° (darkening >115°) (Found: N, 14·2. $C_{15}H_{14}N_4O_7S$ requires N, 14·2%).

Cyclisation of 3-*Acetonyl*-2,4-*dimethylthiazolium Perchlorate with Bases in Aprotic Solvents.—General procedure.* A solution of the salt (5 mmoles) in the solvent (15 ml.) was added to a solution or suspension of the base (5 mmoles, unless otherwise stated) in the same solvent (15 ml.) under nitrogen. The mixture was heated to the specified temperature, stirred for 5 hr. under nitrogen, cooled, and poured into water. The resulting solution was brought to pH 5 by the addition of 0·25M-sulphuric acid before being extracted thrice with ether. The combined extracts were washed free from acid with water and evaporated. The residual oil was steam-distilled, and the distillate was brought to pH 5 before being extracted with ether. The extracts were washed free from acid, dried (Na_2SO_4), and evaporated. The residual oil in ethanol was treated with an excess of perchloric acid. Ether was added to precipitate completely the perchlorate. Details are given in Table 2.

TABLE 2.

Cyclisation of 3-acetonyl-2,4-dimethylthiazolium perchlorate with bases in aprotic solvents.

Solvent	Base	Reaction temp.	Yield (%) *
Dimethylformamide	Sodium acetate	110°	6
,,	,,	145	8
,,	Lithium acetate †	120	6
,,	Potassium cyanide †	120	1
,,	Triethylamine ‡	120	1
Dimethyl sulphoxide	Sodium acetate	60	2
,,	Potassium t-butoxide	60	2

* Isolated as 3,6-dimethyl-5*H*-pyrrolo[2,1-*b*]thiazolium perchlorate. † 10 mmoles. ‡ 7 mmoles.

6-*Acetyl*-3-*methylpyrrolo*[2,1-b]*thiazole.*—A solution of 2,4-dimethylthiazole (11·3 g., 0·1 mole) and bromodiacetyl (16·5 g., 0·1 mole) in chloroform (50 ml.) was boiled for 4 hr., cooled, and extracted with water (2 × 100 ml.). The aqueous extracts were washed with ether (4 × 100 ml.) before being heated with sodium hydrogen carbonate (28 g., 0·33 mole) at 90° for 4 hr. under nitrogen. The mixture was cooled, diluted with water (200 ml.), and extracted with ether. The ether extracts were washed with water, dried (Na_2SO_4), and evaporated. The residue, on being heated at 80—85°/0·1 mm., gave a pale yellow sublimate of 6-*acetyl*-3-*methylpyrrolo*[2,1-b]-*thiazole* (VIId) (2·4 g., 12%). Recrystallisation from acetone–light petroleum (1 : 1) and then from cyclohexane gave colourless needles, m. p. 124—125° (Found: C, 60·1; H, 4·9; N, 7·6; S, 17·3. C_9H_9NOS requires C, 60·3; H, 5·1; N, 7·8; S, 17·9%).

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