Routes to Pyrrolo[2,1-*b*]thiazoles. Rotational Isomerism of Pyrrolo[2,1-*b*]-thiazole-5-carbaldehydes

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Four 3,6-disubstituted pyrrolo[2,1-*b*]thiazoles (one containing a 3-aryl group) were prepared from 2,4-disubstituted thiazoles by the known method, and this work clarified some confusion in the literature. A new route, involving substitution into the thiazole 2-methyl group followed by intramolecular cyclisation and dehydration, gave the 3-methyl-6-phenyl- and 3,6-dimethylpyrrolothiazole in higher yield.

Spectrometric examination of the derived 5-carbaldehydes established the proportions of the *O,N-syn* and *-anti* rotational isomers present and (in two cases) the barrier to rotation of the aldehyde group.

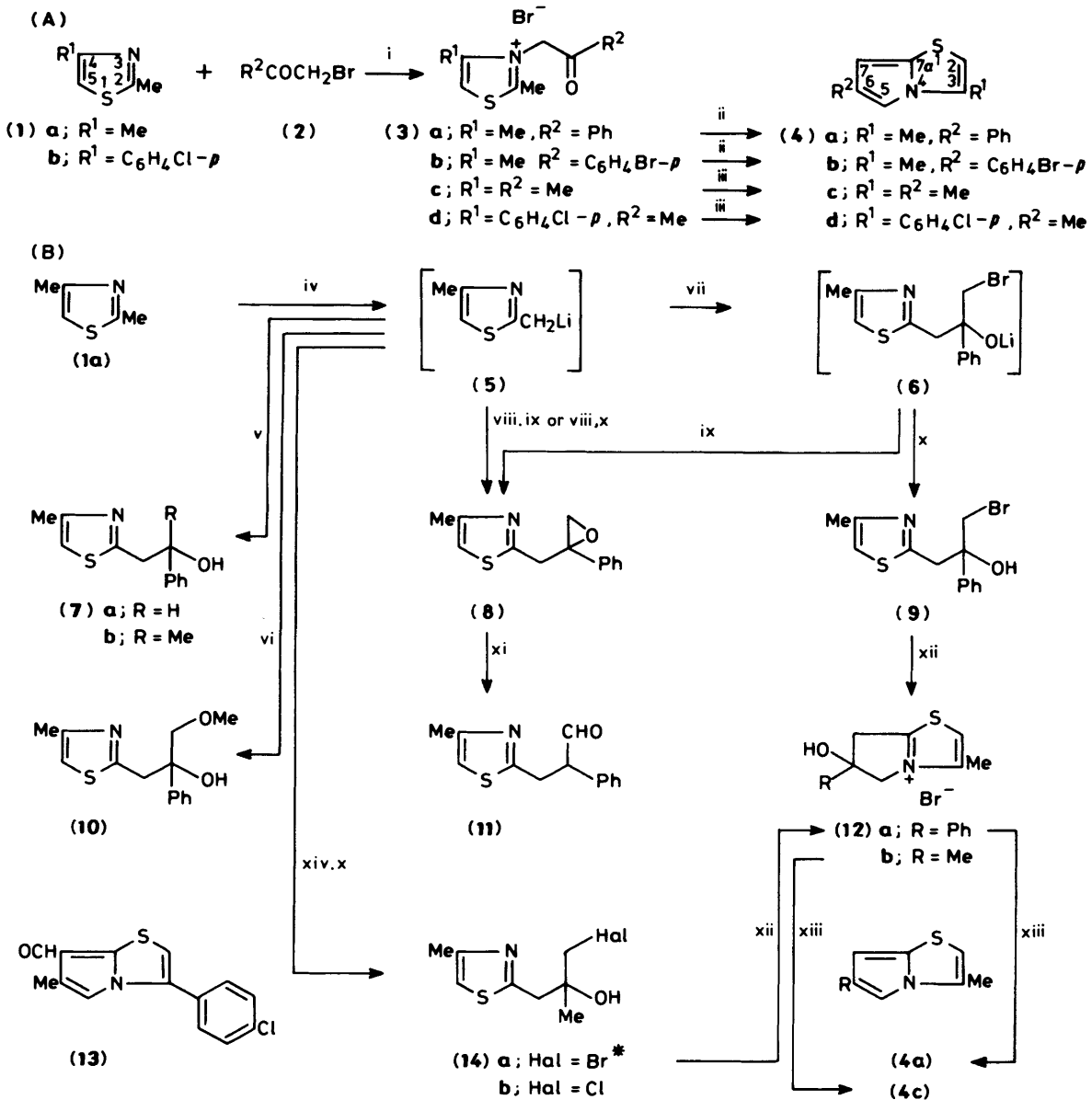
Several studies[1] of pyrrole-2-carbaldehydes lacking polar substituents have established that these compounds have a marked or even an exclusive preference for the carbonyl *O,N-syn* conformation; the standard ^{1}H n.m.r. approach to measuring the rotational barrier of the aldehyde group is thereby excluded and a special technique was used[2] with the only simple compound (*N*-methylpyrrole-2-carbaldehyde) for which this feature has been assessed. The present work on 3,6-disubstituted pyrrolo[2,1-*b*]thiazole-5-carbaldehydes (in which the aldehyde group is also at the α-position of the pyrrole ring) was prompted by two considerations: a suitable combination of 3- and 6-substituents should produce a balanced situation with appreciable amounts of both isomers present, and, as discussed later, the operation of a mesomeric effect should increase the aldehyde group's rotational barrier and thereby facilitate detection of the rotamers.

The previous preparative work on pyrrolo[2,1-*b*]thiazoles is based on the route[3] by which the first representative, the 3-methyl-6-phenyl derivative, was obtained. Subsequently this route was developed simultaneously in two laboratories and gave series of products containing either a 6-aryl group[4] or a 6-methyl group.[5] Thus all the known pyrrolothiazoles have been prepared by the sequence shown (for the 3,6-substituted compounds) in section A of the Scheme and (see later) it is significant that only thiazoles without a 4-substituent or with a 4-methyl group have been used as starting materials. Quaternisations with 2-bromoacetophenone and its derivatives proceeded readily[4,5a] but some of those involving bromoacetone were appreciably more difficult.[5a] Cyclisation of the salts (**3**; R^2 = Ar) from aromatic bromo ketones by treatment with sodium carbonate or hydroxide in water or aqueous methanol was stated[4] to give 6-arylpyrrolothiazoles (**4**; R^2 = Ar) in yields of 17—59% from the thiazoles (**1**). In contrast, Reid and co-workers reported[5a] a low yield of the pyrrolothiazole (**4a**) from cyclisation of the salt (**3a**) with aqueous sodium carbonate (*cf.* 36% recorded[4]); cyclisations of the salt (**3**; R^1 = H, R^2 = Ph) with aqueous solutions of several inorganic bases also gave low yields, and these reagents were found to be even less efficient with a salt (**3**; R^1 = H, R^2 = Me) derived from bromoacetone. A different cyclisation procedure was therefore developed: heating the salts with sodium acetate in acetic anhydride gave acetyl derivatives of the pyrrolothiazoles from which the parent compounds were obtained by acid-catalysed deacetylation. This method was reported[5] to be suitable for both types of salt (*i.e.*, those from phenacyl bromide and those from bromoacetone).

In the present work cyclisation of the salt (**3a**) with aqueous sodium carbonate was found to be unsatisfactory but the use of methanolic sodium hydroxide gave the pyrrolothiazole (**4a**) in an overall yield of 33%. Similarly, product (**4b**) was obtained in a yield of 44% (*cf.* 45% recorded[4]). The salt (**3c**) could not be cyclised in this way but, in agreement with Reid and co-workers,[5a] the alternative procedure afforded the dimethylpyrrolothiazole (**4c**) satisfactorily [yield of 44% from the thiazole (**1a**)]. For the development of the spectrometric work it was desirable to prepare a pyrrolothiazole with an aromatic group at position 3, a type hitherto unknown. As expected from kinetic studies[6] of the reactions between 4-substituted thiazoles and methyl iodide, quaternisation of a 4-arylthiazole with bromoacetone proved difficult. Even under forcing conditions 4-(4-chlorophenyl)-2-methylthiazole (**1b**)[7] gave only a low yield (22%) of the salt (**3d**) which was characterised as the corresponding perchlorate and then cyclised to the 3-(4-chlorophenyl)pyrrolothiazole (**4d**).

Since the overall yields of the two stages in route A are generally less than 50% a new approach (section B of Scheme) was envisaged. Substitution of a suitably functionalised C_2-unit into the thiazole 2-methyl group was to give an intermediate which by cyclisation (facilitated by being intramolecular) and then dehydration (favoured by forming an aromatic system) would give a pyrrolothiazole. 4-Alkyl-2-methylthiazoles undergo selective deprotonation of the 2-methyl group at −78 °C but at higher temperatures dimeric products are formed.[8] The feasibility of the approach was tested by treating the lithio derivative of 2,4-dimethylthiazole (**1a**) with benzaldehyde and with acetophenone at low temperature: reaction occurred clearly at the 2-methyl group to give products (**7**). It was then necessary to find a 2-substituted acetophenone $PhCOCH_2X$ which would undergo nucleophilic addition by the lithio derivative (**5**) to give an intermediate suitable for cyclisation and dehydration. (One obvious problem, that of proton abstraction from the potentially acidic methylene group, did not occur with any of the substituted acetophenones used here.) 2-Methoxyacetophenone[9] (X = OMe) gave product (**10**) efficiently but attempts to convert this into the pyrrolothiazole (**4a**) directly by treatment with hydrogen bromide were unsuccessful. With X = OTs [2-(*p*-tolylsulphonyloxy)-acetophenone[10]] the group leaves too readily; the epoxide (**8**) was formed, even at −55 °C, and under acidic conditions this underwent rearrangement to the aldehyde (**11**) rather than the desired ring-opening to an α-diol. A suitable intermediate was obtained by using 2-bromoacetophenone (X = Br) under controlled conditions. When the adduct (**6**) was allowed to come to 20 °C the epoxide (**8**) was obtained, but work-up at −55 °C led to the bromohydrin (**9**). Cyclisation and dehydration under mild conditions afforded 3-methyl-6-phenylpyrrolo[2,1-*b*]thiazole in 65% overall yield from 2,4-

Scheme. Preparation of pyrrolo[2,1-*b*]thiazoles.



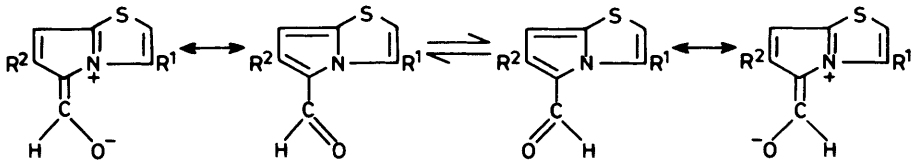
Reagents and conditions: i, Heat, alone or in a solvent; ii, NaOH–MeOH, heat; iii, NaOAc–Ac_2O, heat, then HCl–H_2O, heat; iv, BuLi–THF, −70 °C; v, PhCOR, −55 °C; vi, $PhCOCH_2OMe$, −55 °C; vii, $PhCOCH_2Br$, −55 °C; viii, $PhCOCH_2OTs$, −55 °C; ix, Warm to 20 °C, then AcOH; x, AcOH, −55 °C; xi, $HClO_4$–H_2O–Me_2CO; xii, Me_2CO, heat; xiii, NaOH–H_2O–MeOH; xiv, $MeCOCH_2Hal$, −55 °C.
* Not fully characterised

dimethylthiazole (**1a**). Similarly, using bromoacetone, the 3,6-dimethyl compound (**4c**) was obtained (63%). [Cyclisation of the chloro intermediate (**14b**) was unsatisfactory.] It may be that the intramolecular cyclisation involved in route B will be advantageous in the preparation of 3-aryl compounds.

Pyrrolo[2,1-*b*]thiazoles undergo electrophilic substitution readily,[4] first at position 5 then at position 7.[11] Three 5-carbaldehydes have been described: the Vilsmeier reaction with 6-methyl- and 6,7-dimethyl-pyrrolothiazole gives the 5-formyl derivatives and, from the former substrate, the 5,7-diformyl product.[11] The presumption that formylation of the pyrrolothiazoles (**4b—d**) would occur at position 5 was confirmed[12] by ^{1}H n.m.r. comparisons between the products (**15b—d**) and the starting materials; further, the 6-(*p*-chlorophenyl) compound (**4d**) gave, as a minor product, the isomeric 7-carbaldehyde (**13**) (Scheme).

The Table shows the spectrometric results relevant to rotational isomerism of the 5-carbaldehydes. In non-polar solvents the aldehyde (**15b**) exists predominantly in one form over the temperature range studied; on steric grounds this is likely to be the *O,N-syn* conformation. Below about −30 °C the ^{1}H n.m.r. spectra (source frequency 90 MHz) of the other two (**15c** and **d**) show that both rotational isomers are present. The isomers with the lower-field aldehyde signals have relative deshielded 6-methyl groups; in the isomer of the 3,6-dimethyl compound (**15c**) with the higher-field aldehyde signal the 3-methyl group is deshielded. Consideration of the anisotropic effects of the carbonyl double bonds on the methyl groups then leads to the assignments shown in the Table. For two compounds (**15b** and **c**), an increase in solvent polarity is seen to decrease the amounts of the forms with higher wavenumbers. Identification of these forms as the *syn* isomers, in which

Table. I.r. and ^{1}H n.m.r. absorptions of pyrrolo[2,1-*b*]thiazole-5-carbaldehydes. The positions of i.r. bands (cm^{-1}) and ^{1}H n.m.r. signals (δ values) assigned to particular rotational isomers are followed, in parentheses, by the percentage areas of the absorptions.[a] The $\Delta G^{\ddagger}$ values (kJ mol^{-1}; statistical error ±3 kJ mol^{-1}) are the activation energies for rotation about the C(5)–CHO bond at 298 K



Compound	Temp. (K)	Solvent	*O,N-syn*			*O,N-anti*			$\Delta G^{\ddagger}$
(**15b**; R^1 = Me, R^2 = C_6H_4Br-*p*)	I.r. 303	CCl_4	1 656 (100)						
	I.r. 303	MeCN	1 649 (85)			1 630 (15)			
	^{1}H n.m.r. 305	CD_2Cl_2	CHO	C_6H_4	3-Me				
			9.32s	7.43m	2.83d				
	208	CD_2Cl_2	9.21s	7.42m	2.73d				
(**15c**; R^1 = R^2 = Me)	I.r. 303	CCl_4	1 655 (75)			1 648 (25)			52
	I.r. 303	MeCN	1 648 (60)			1 634 (40)			
	^{1}H n.m.r 305	CD_2Cl_2		CHO		3-Me	6-Me		
				9.75s		2.70d	2.40s		
	208	CD_2Cl_2	CHO	3-Me	6-Me	CHO	3-Me	6-Me	
			10.09s (55)	2.62d (54)	2.42s (55)	9.36s (45)	2.74d (46)	2.38s (45)	
(**15d**; R^1 = C_6H_4Cl-*p*, R^2 = Me)	I.r. 303	CCl_4	*ca.* 1 661[b]			1 654			49
	I.r. 303	MeCN	1 656 (30)			1 644 (70)			
	^{1}H n.m.r. 305	CD_2Cl_2		CHO		C_6H_4	6-Me		
			9.34s			7.41m	2.48s		
	208	CD_2Cl_2	CHO	C_6H_4	6-Me	CHO	C_6H_4	6-Me	
			9.42s(25)	7.35m (26)	2.50s (24)	9.27s(75)	7.46m (24)	2.46s (76)	

[a] Work as, or referred to, in ref. 14. [b] Inflexion on main band, area uncertain.

intramolecular electrostatic interaction is to be expected, harmonises the ^{1}H n.m.r. and i.r. results. Comparison of the 3,6-dimethyl-5-carbaldehyde (**15c**) with *N*-methylpyrrole-2-carbaldehyde [which has a barrier to rotation[2] (at 298 K) of 48 kJ mol^{-1} and exists as the *syn* form,[13] $\nu_{max.}(CCl_4)$ 1 668; $\nu_{max.}$(MeCN) 1 664 cm^{-1}] confirms that the mesomeric effect is more pronounced in the pyrrolothiazole system.

Experimental

Spectra were recorded as specified earlier.[14] Complete spectrometric characteristics of products are given elsewhere.[12] Light petroleum refers to the fraction with b.p. 40—60 °C, and THF to tetrahydrofuran.

Work in Section A of Scheme.—A stirred mixture of 2,4-dimethylthiazole[15] (**1a**) (4.52 g) and phenacyl bromide (7.96 g) was heated on the steam-bath for 1 h. The product was powdered, washed with Me_2CO, and crystallised from EtOH to give 2,4-*dimethyl*-3-*phenacylthiazolium bromide* (**3a**) (10.42 g), m.p. 215—218 °C (decomp.) (Found: C, 49.9; H, 4.5. $C_{13}H_{14}$BrNOS requires C, 50.0; H, 4.5%); $\nu_{max.}$(Nujol) 1 690 cm^{-1}.

A solution of this salt (4.69 g) in 10M-NaOH (2 ml)–MeOH (100 ml) was boiled under reflux for 30 min, and the volume was then reduced to *ca.* 50 ml at 40 °C/20 mmHg. The material precipitated by the addition of water (100 ml) to the cold solution was collected, dried, and crystallised from EtOH to give the pyrrolothiazole (**4a**) (1.25 g), m.p. 70—71 °C (lit.,[4] 71 °C). Similarly, 2,4-dimethylthiazole (4.52 g) and 4-bromophenacyl bromide (11.2 g) gave the salt (**3b**) (13.8 g), m.p. 210—213 °C (decomp.) (from Pr^iOH) (lit.,[4] 213 °C), a portion (6.23 g) of which was converted into the pyrrolothiazole (**4b**) (2.34 g), m.p. 119—121 °C (from EtOH) (lit.,[4] 121 °C). The published procedures,[5a] using 2,4-dimethylthiazole (4.9 g) and bromoacetone (5.25 g), afforded the pyrrolothiazole (**4c**) (2.9 g), b.p. 126—130 °C/15 mmHg (lit.,[5a] 105—110 °C/10 mmHg). The instability of this compound has been reported.[5a] It darkens rapidly in air at 20 °C but can be stored *in vacuo* at 0 °C in the dark.

Work in Section B of Scheme.—Products (**7a**), (**7b**), *and* (**10**). A 1.56M-solution of Bu^nLi in hexane (11 ml) was added during 5 min to a solution of 2,4-dimethylthiazole (**1a**) (1.8 g) in THF (35 ml) which was stirred under N_2 at −70 °C during the addition, and then for a further 15 min. A solution of benzaldehyde (1.69 g) in THF (15 ml) was added during 10 min, and the mixture was stirred for a further 1 h at −55 °C. The cooling bath was removed, and after 1.5 h the mixture was poured into 2M-aqueous Na_2CO_3. Extraction with EtOAc gave 2-(4-*methylthiazol*-2-*yl*)-1-*phenylethanol* (**7a**) (2.98 g), b.p. 97—99 °C/0.5 mmHg, m.p. 87—88 °C (from CCl_4) (Found: C, 65.6; H, 6.0; N, 6.4. $C_{12}H_{13}NOS$ requires C, 65.7; H, 6.0; N, 6.4%); $\nu_{max.}$ (dilute solution in CCl_4, 1 cm cell) 3 604 sharp (free OH) and 3 380br cm^{-1} (intramolecularly bonded OH); δ_H (2.36, 3 H, d, *J* 1.2 Hz, 4-Me) [*cf.* 2,4-dimethylthiazole (**1a**), δ_H 2.59 (3 H, s, 2-Me), and 2.34 (3 H, d, *J* 1.1 Hz, 4-Me)].

A similar experiment using Bu^nLi (4.2 ml), the thiazole (**1a**) (0.68 g), and acetophenone (0.72 g) afforded material which was purified by flash chromatography with CH_2Cl_2–Et_2O (19:1) as eluant to give 1-(4-*methylthiazol*-2-*yl*)-2-*phenylpropan*-2-*ol* (**7b**) (1.12 g), m.p. 64—66 °C (Found: C, 67.1; H, 6.4; N, 5.9. $C_{13}H_{15}NOS$ requires C, 66.9; H, 6.5; N, 6.0%).

Similarly, Bu^{n}Li (2.91 ml), the thiazole (**1a**) (0.46 g), and 2-methoxyacetophenone (0.61 g), and distillation of the product, gave 1-*methoxy*-3-(4-*methylthiazol*-2-*yl*)-2-*phenylpropan*-2-*ol* (**10**) (0.96 g), b.p. 102—105 °C/0.05 mmHg (Found: M^+, 263.0981. $C_{14}H_{17}NO_2S$ requires M, 263.0980).

Products (**9**), (**8**), (**11**), (**14a**), *and* (**14b**). A 1.56M-solution of Bu^{n}Li in hexane (7.0 ml) was added during 5 min to a solution of 2,4-dimethylthiazole (**1a**) (1.13 g) in THF (20 ml) which was stirred under N_2 at −70 °C during the addition and then for a further 15 min. A solution of phenacyl bromide (2.0 g) in THF (10 ml) was added during 10 min, the mixture was then stirred for 1.5 h at −55 °C, and a solution of acetic acid (1.8 ml) in THF (5 ml) was added during 5 min. The cooling bath was removed, and after 1 h the solution was poured into water. Basification with 2M-aqueous Na_2CO_3, extraction with Et_2O, and purification by flash chromatography with CH_2Cl_2–Et_2O (9:1) as eluant gave 1-*bromo*-3-(4-*methylthiazol*-2-*yl*)-2-*phenylpropan*-2-*ol* (**9**) (2.51 g) (Found: C, 50.2; H, 4.4; N, 4.5. $C_{13}H_{14}BrNOS$ requires C, 50.0; H, 4.5; N, 4.5%); m/z 312 (M^+, 11%), 232 (39), and 113 (100).

The foregoing experiment was repeated using Bu^{n}Li (6.4 ml), the thiazole (**1a**) (1.03 g), and phenacyl bromide (1.82 g), but the cooling bath was removed and the solution was allowed to warm to 20 °C before the addition of acetic acid (1.65 ml) in THF (5 ml). Work-up as before gave material which was chromatographed on neutral Al_2O_3 (100 g). Hexane–benzene (4:1) eluted 2-(2,3-*epoxy*-2-*phenylpropyl*)-4-*methylthiazole* (**8**) as an oil (1.58 g) (Found: C, 67.3; H, 5.6; N, 6.2. $C_{13}H_{13}NOS$ requires C, 67.5; H, 5.7; N, 6.1%); δ_H 7.33 (5 H, m, Ph), 6.69 (1 H, q, J 1.2 Hz, 5-H), 3.77 and 3.53 (2 H, two d, J 16 Hz, 1′-H_2), 3.05 and 2.75 (2 H, two d, J 4.8 Hz, 3′-H_2), and 2.34 (3 H, d, J 1.2 Hz, 3-Me); m/z 231 (M^+, 100%).

The procedure for preparing compound (**9**) was used with Bu^{n}Li (2.85 ml), the thiazole (**1a**) (0.46 g), and 2-(*p*-tolylsulphonyloxy)acetophenone (1.18 g). This gave the epoxide (**8**) (0.72 g). A further such experiment in which the reaction mixture was allowed to warm to 20 °C before the addition of acetic acid also gave the epoxide (**8**) (78%).

A solution of the foregoing epoxide (**8**) (241 mg) and 6M-aqueous $HClO_4$ (0.8 ml) in acetone (10 ml) was kept at 20 °C for 4 h. The residue obtained by evaporation at 20 °C/15 mmHg was dissolved in ethyl acetate, and the solution was washed with 2M-aqueous Na_2CO_3, and dried. After evaporation of the solvent the residue was chromatographed on neutral Al_2O_3 (30 g). Elution with hexane–benzene (3:1) gave 3-(4-*methylthiazol*-2-*yl*)-2-*phenylpropionaldehyde* (**11**) as an oil (218 mg) (Found: M^+, 231.0718. $C_{13}H_{13}NOS$ requires M^+, 231.0718); δ_H 9.68 (1 H, s, CHO); $\nu_{max.}$ 1 728 cm^{-1}.

The procedure for preparing compound (**9**) was used with Bu^{n}Li (7.0 ml), the thiazole (**1a**) (1.13 g), and bromoacetone (1.37 g). The product consisted of a viscous oil and a small amount of a solid. On trituration with dry ether the solid remained undissolved. Evaporation of the ether phase gave an oil (1.98 g) [δ_H 6.70 (1 H, q, J 1.1 Hz, 5′-H), *ca.* 4.9 (1 H, br, OH), 3.25 (4 H, m, 1- and 3-H_2), 2.39 (3 H, s, 4′-Me), and 1.38 (3 H, s, 2-Me)] formulated as 1-bromo-2-methyl-3-(4-methylthiazol-2-yl)propan-2-ol (**14a**).

The procedure for preparing compound (**9**) was used with Bu^{n}Li (7.0 ml), the thiazole (**1a**) (1.13 g), and chloroacetone (0.93 g). The product was purified by flash chromatography with CH_2Cl_2–Et_2O (9:1) as eluant; distillation of the residual product at *ca.* 40 °C/0.1 mmHg gave 1-*chloro*-2-*methyl*-3-(4-*methylthiazol*-2-*yl*)*propan*-2-*ol* (**14b**) (1.42 g), m.p. 65—67 °C (Found: C, 46.7; H, 6.0; N, 6.9. $C_8H_{12}ClNOS$ requires C, 46.7; H, 5.9; N, 6.8%); m/z 206 (M^+, 95%) and 113 (100).

Products (**12a**), (**12b**), (**4a**), *and* (**4c**). A solution of the bromo-compound (**9**) (2.1 g) in acetone (120 ml) was boiled under reflux for 2 days, and cooled. The insoluble material was collected, and washed with acetone. Crystallisation from cyclopropane gave 6,7-*dihydro*-6-*hydroxy*-3-*methyl*-6-*phenyl*-5H-*pyrrolo*[2,1-b]*thiazolium bromide* (**12a**) (1.86 g), m.p. 181—183 °C (Found: C, 50.1; H, 4.6; N, 4.5. $C_{13}H_{14}BrNOS$ requires C, 50.0; H, 4.5; N, 4.5%).

Similarly, the oil (1.98 g) formulated as the bromo-compound (**14a**) gave 6,7-*dihydro*-6-*hydroxy*-3,6-*dimethyl*-5H-*pyrrolo*[2,1-b]*thiazolium bromide* (**12b**) (1.88 g), m.p. 222—223 °C (decomp.) (from PrOH) (Found: C, 38.6; H, 5.0; N, 5.7. $C_8H_{12}BrNOS$ requires C, 38.4; H, 4.8; N, 5.6%).

A solution of the bromide (**12a**) (510 mg) in 10M-aqueous NaOH (20 ml)–MeOH (20 ml) was stirred at 20 °C for 4 h, and then poured into brine (50 ml). Extraction with ether gave the pyrrolothiazole (**4a**) (325 mg), m.p. and mixed m.p. 69—70 °C. Similarly the bromide (**12b**) (420 mg) gave the pyrrolothiazole (**4c**) (212 mg), identified by comparison (i.r. and ^{1}H n.m.r.) with an authentic specimen.

The Aldehydes (**15b**), (**15c**), (**15d**), *and* (**13**).—A solution of phosphoryl trichloride (332 mg) in dimethylformamide (DMF) (5 ml) was added during 30 min to a solution of the pyrrolothiazole (**4b**) (610 mg) in DMF (15 ml) which was stirred at −35 °C during the addition and then for a further 30 min. The mixture was poured into ice–water (50 ml), and basified with 2M-aqueous Na_2CO_3. The material isolated with ether was purified by flash chromatography with CH_2Cl_2–Et_2O (9:1) as eluant to give 6-(4-*bromophenyl*)-3-*methylpyrrolo*[2,1-b]-*thiazole*-5-*carbaldehyde* (**15b**) (522 mg), m.p. 142—144 °C (from cyclohexane) (Found: C, 52.4; H, 3.2; N, 4.4. $C_{14}H_{10}BrNOS$ requires C, 52.5; H, 3.15; N, 4.4%).

This procedure with the pyrrolothiazole (**4c**) (450 mg) gave 3,6-*dimethylpyrrolo*[2,1-b]*thiazole*-5-*carbaldehyde* (**15c**) (432 mg), m.p. 82—84 °C (Found: C, 60.1; H, 5.0; N, 7.9. C_9H_9NOS requires C, 60.3; H, 5.1; N, 7.8%); m/z 179 (M^+, 100%).

Similarly, the pyrrolothiazole (**4d**) (1.31 g) gave material which was separated by flash chromatography, with CH_2Cl_2–Et_2O (9:1) as eluant, into two fractions. The first was 3-(4-*chlorophenyl*)-6-*methylpyrrolo*[2,1-b]*thiazole*-5-*carbaldehyde* (**15d**) (1.14 g), m.p. 146—147 °C (from EtOH) (Found: C, 60.9; H, 3.8; N, 5.1. $C_{14}H_{10}ClNOS$ requires C, 61.0; H, 3.7; N, 5.1%); δ_H 6.25 (1 H, s, 7-H); m/z 275 (M^+, 100%). The second was 3-(4-*chlorophenyl*)-6-*methylpyrrolo*[2,1-b]*thiazole*-7-*carbaldehyde* (**13**) (0.17 g), m.p. 188—189 °C [from Et_2O–light petroleum (1:5)] (Found: C, 60.9; H, 3.4; N, 5.2%); δ_H 7.02 (1 H, s, 5-H); m/z 275 (M^+, 100%).

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References

1 B. P. Roques and S. Combrisson, *Can. J. Chem.*, 1973, **51**, 573; D. J. Chadwick, G. D. Meakins, and E. E. Richards, *Tetrahedron Lett.*, 1974, 3183; M. Farnier and T. Drakenberg, *J. Chem. Soc., Perkin Trans. 2*, 1975, 333.
2 L. Arlinger, K. Dahlqvist, and S. Forsen, *Acta Chem. Scand.*, 1970, **24**, 662.
3 H. Kondo and F. Nagasawa, *J. Pharm. Soc. Jpn.*, 1937, **57**, 1050.
4 T. Pyl, H. Gille, and D. Nusch, *Justus Liebigs Ann. Chem.*, 1964, **679**, 139.
5 (*a*) B. B. Molloy, D. H. Reid, and F. S. Skelton, *J. Chem. Soc.*, 1965, 65; (*b*) R. K. Mackie, S. McKenzie, D. H. Reid, and R. G. Webster, *J. Chem. Soc., Perkin Trans. 1*, 1973, 657.
6 G. B. Behera, J. N. Kar, R. C. Acharga, and M. K. Rout, *J. Org. Chem.*, 1973, **38**, 2164.
7 J. P. Wetherill and R. M. Hann, *J. Am. Chem. Soc.*, 1934, **56**, 970.
8 G. Knaus and A. I. Meyers, *J. Org. Chem.*, 1974, **39**, 1192.
9 M. S. Newmann and P. B. Neal, *J. Am. Chem. Soc.*, 1950, **72**, 5161.
10 A. L. Crowther and G. Holt, *J. Chem. Soc.*, 1963, 2818.

11 S. McKenzie, B. B. Molloy, and D. H. Reid, *J. Chem. Soc. C*, 1966, 1908.
12 D. W. Gillon, D.Phil. Thesis, Oxford, 1983.
13 P. T. Kaye, R. Macrae, G. D. Meakins, and C. H. Patterson, *J. Chem. Soc., Perkin Trans. 2*, 1980, 1631.
14 D. W. Gillon, I. J. Forrest, G. D. Meakins, M. D. Tirel, and J. D. Wallis, *J. Chem. Soc., Perkin Trans. 1*, 1983, 341.
15 N. I. Fisher and F. M. Hamer, *J. Chem. Soc.*, 1930, 2509.

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