805. *Nuclear Magnetic Resonance. Part III.*[1] *The Structure of Pyrrolo*[2,1-b]*thiazolium Cations*

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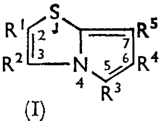
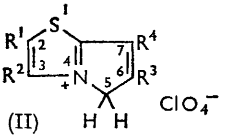
Pyrrolo[2,1-*b*]thiazoles give stable crystalline salts with acids. The structure of the pyrrolo[2,1-*b*]thiazolium cations has been determined by a proton magnetic resonance study of pyrrolo[2,1-*b*]thiazoles and their perchlorates in trifluoroacetic acid. Protonation of pyrrolo[2,1-*b*]thiazoles occurs preferentially at position 5. Exceptionally, 5,6-dimethylpyrrolo-[2,1-*b*]thiazole forms a mixture of the 5*H*- and 7*H*-cations in which the former predominates.

Pyrrolo[2,1-*b*]thiazoles (I) dissolve reversibly in aqueous solutions of strong acids, and with perchloric or picric acid[2] afford stable crystalline salts. This Paper describes the preparation and a study of the structure of pyrrolo[2,1-*b*]thiazolium perchlorates by proton magnetic resonance spectroscopy. Solutions of the pyrrolo[2,1-*b*]thiazoles in trifluoroacetic acid were also examined. The site of protonation was determined comparatively by studying the effect of substitution in the pyrrolo[2,1-*b*]thiazolium cation on the occurrence of signals and their multiplicity due to spin–spin coupling.

	R^1	R^2	R^3	R^4	R^5
a:	H	H	H	H	H
b:	H	H	H	Me	H
c:	H	H	H	Me	Me
d:	H	H	Me	Me	Me
e:	H	H	Me	Me	H



(I)



(II)

	R^1	R^2	R^3	R^4
a:	H	H	H	H
b:	H	H	Me	H
c:	H	H	Me	Me
d:	Me	H	Me	H
e:	H	Me	Me	H
f:	H	Me	Me	Me
g:	H	Me	Me	Ph
h:	H	H	Ph	H
i:	Me	H	Ph	H
j:	H	Me	Ph	H

None of the spectra of the pyrrolo[2,1-*b*]thiazoles or their perchlorates in trifluoroacetic acid shows a broad band or triplet which would arise from a proton bonded to nitrogen. The pattern of the spectra also excludes sulphur as the site of protonation. Protonation at carbon occurs with the formation of a methylene or substituted methylene group.

We compare first the spectra (see Figure) of pyrrolo[2,1-*b*]thiazolium perchlorate (IIa) (A) 6-methylpyrrolo[2,1-*b*]thiazolium perchlorate (IIb) (B), 6,7-dimethylpyrrolo[2,1-*b*]-thiazolium perchlorate (IIc) (C), and 5,6,7-trimethylpyrrolo[2,1-*b*]thiazolium perchlorate (III) (D). The integrated spectrum of the parent salt (IIa) shows three features. (i) A

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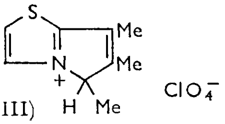
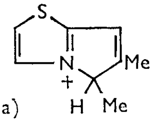
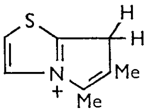
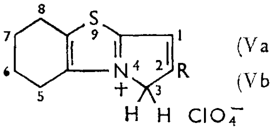
[2] B. B. Molloy, D. H. Reid, and (in part) F. S. Skelton, *J.*, 1965, 65.

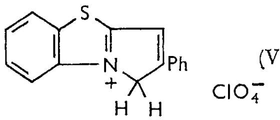
single peak (2H) occurs at δ 5·38. This is assigned to a methylene group on the basis of its spectral position. (ii) Two doublets (2H) with equally spaced components occur at δ 7·93 and 8·36 (J = 4·0 c./sec.), and clearly arise from an AB system of two protons.


(III)

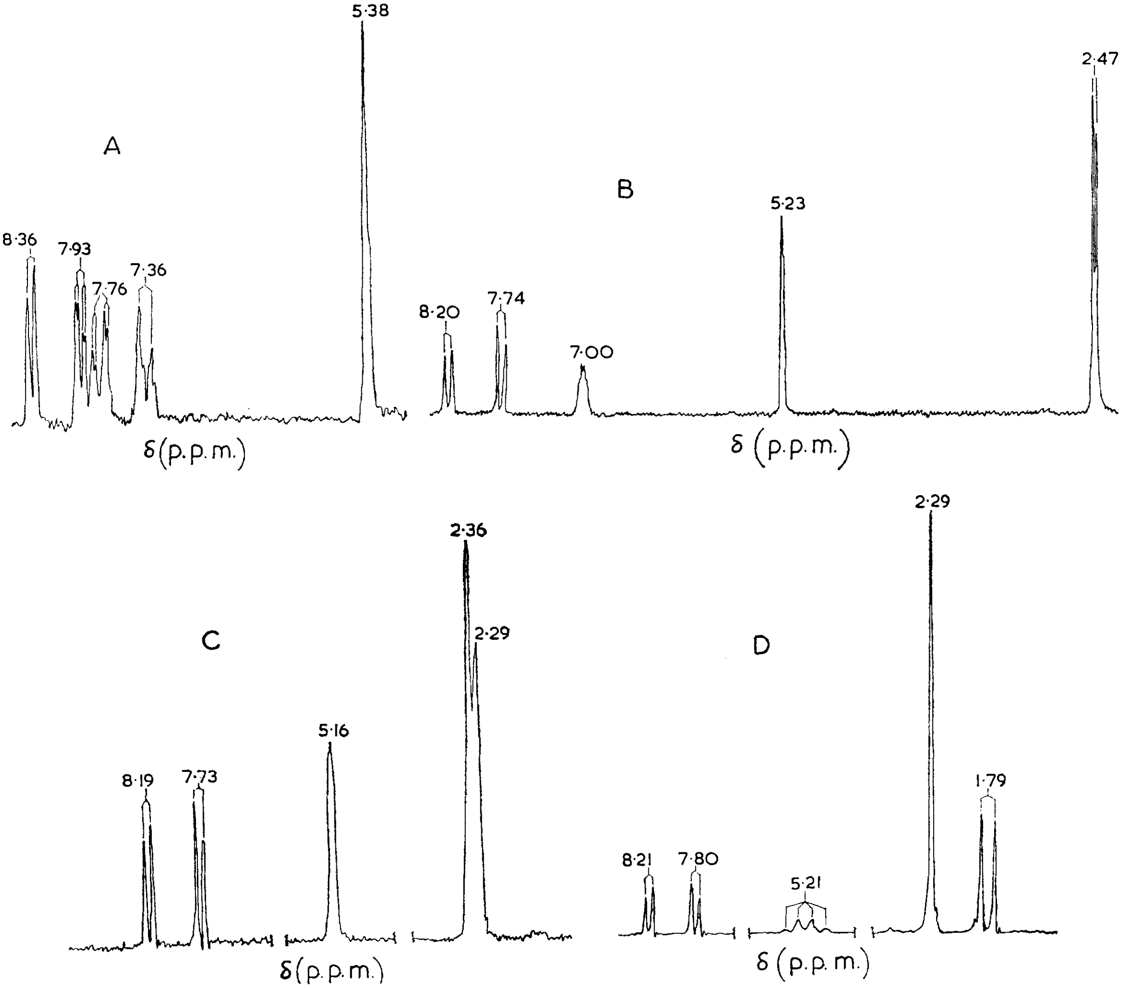

(IVa)


(IVb)


(Va: R = Me)
(Vb: R = Ph)


(VI)

(iii) A further two doublets (2H) due to a second AB pair occur at δ 7·76 and 7·36 (J = 6·3 c./sec.). (There is some smaller splitting of these lines which is discussed later.) Two features of the spectrum of this salt are also found in the spectra of 6-methyl- (IIb) and 6,7-dimethyl-pyrrolo[2,1-*b*]thiazolium perchlorate (IIc). First, the spectra of the salts (IIb and c) show singlets (2H) at δ 5·23 and 5·16. Secondly, they also show an AB



system corresponding to that at low field in the spectrum of (IIa), with slightly increased shielding. The spectrum of 5,6,7-trimethylpyrrolo[2,1-*b*]thiazolium perchlorate (III) shows one feature common to the spectra of the salt (IIa—c), namely, the low-field AB system.

The pattern of the low-field signals is thus unaltered by the progressive introduction of methyl groups at positions 6, 7, and 5. The low-field AB system common to the spectra of all four salts (IIa—c) and (III) can only arise from H-2 and H-3. Therefore these salts must have resulted from protonation of the pyrrolo[2,1-*b*]thiazoles (Ia—d) in the pyrrole ring. In the case of 6,7-dimethylpyrrolo[2,1-*b*]thiazole(Ic) a methylene group can develop on protonation only at position 5. Also, since the signals from the methylene protons of the salts (IIa and b) occur in the same narrow spectral range (δ 5·16—5·38) as that from the methylene protons of 6,7-dimethylpyrrolo[2,1-*b*]thiazolium perchlorate, we conclude that pyrrolo[2,1-*b*]thiazolium perchlorate and 6-methylpyrrolo[2,1-*b*]thiazolium perchlorate also result from protonation at position 5. The signal of a methylene group resulting from protonation at position 7 would be expected to lie considerably upfield of that from a 5-methylene group, since the latter is directly linked to the positively charged nitrogen atom. In fact, the 7-methylene signal of the 5,6-dimethyl-7*H*-pyrrolo[2,1-*b*]thiazolium cation (IVb) occurs at δ 4·15.

The spectrum of 5,6,7-trimethylpyrrolo[2,1-*b*]thiazolium perchlorate (III) shows a quartet centred at δ 5·21 (1H) in place of the methylene singlets in the spectra of the perchlorates (IIa—c). The multiplicity arises from coupling of this proton with a methyl group linked to the same carbon atom. This is confirmed by the presence of a doublet (3H) centred at δ 1·79, showing the same splitting (J = 7·2 c./sec.). Since the quartet occurs in the same region as the methylene signals of the salts (IIa—c) we conclude that 5,6,7-trimethylpyrrolo[2,1-*b*]thiazole (Id) is also protonated at position 5.

The interpretation of the remaining features of the spectra of the perchlorates (IIa—c) and (III) agree with the foregoing conclusions (details are given in the Table). Two features deserve further comment. First, the higher-field AB pair of doublets in the spectrum of (IIa) is assigned to H-6 and H-7 because (i) one of the doublets (δ 7·36) falls in the same region as the H-7 singlet of other pyrrolo[2,1-*b*]thiazolium perchlorates, (ii) the coupling between H-6 and H-7 (J = 6·3 c./sec.) is much greater than that (J = 4 c./sec.) found for the H-2, H-3 interaction in other 6-methylpyrrolo[2,1-*b*]thiazolium perchlorates. The high-field components centred at δ 7·36 are assigned to H-7 on the basis of comparisons with the H-7 signals of other salts. Secondly, the low-field doublet of the AB system arising from H-2 and H-3 is assigned to H-3 on account of its proximity to the more electronegative hetero-atom. The chemical shifts of H-3 in 2,6-dimethyl- (IId) and H-2 in 3,6-dimethylpyrrolo[2,1-*b*]-thiazolium perchlorate (IIe) (Table) agree well with this assignment.

Spectral assignments for eight other pyrrolo[2,1-*b*]thiazolium salts (IIf—j), (Va and b), and (VI) have been made on the basis of the foregoing results. All are in agreement with protonation at position 5.

The spectra of the perchlorates (IIa—f) and (III) were identical in pattern with those of the corresponding bases in trifluoroacetic acid. This establishes that the salts (IIa—f) and (III) are the only protonation products formed in measurable amount. However, the 7*H*-pyrrolo[2,1-*b*]thiazolium cations must co-exist with the 5*H*-cations when the bases are dissolved in trifluroacetic acid, but at concentrations below the limit of detection by proton magnetic resonance spectroscopy, because solutions of 6-methyl-, 6,7-dimethyl, 5,6,7-trimethyl-, and 6-phenyl-pyrrolo[2,1-*b*]thiazole in deuterotrifluoroacetic acid showed rapid exchange of hydrogen at both positions 5 and 7. In contrast, the spectra of the perchlorates of these bases in trifluoroacetic and deuterotrifluoroacetic acid were identical, thus showing that the 5-methylene protons of pyrrolo[2,1-*b*]thiazolium perchlorates do not exchange at a detectable rate with the solvent.

Some weak couplings in the spectra of the pyrrolo[2,1-*b*]thiazolium perchlorates were further examined. In the spectrum of pyrrolo[2,1-*b*]thiazolium perchlorate (IIa) the

Chemical shifts in the proton magnetic resonance spectra of (A) pyrrolo[2,1-*b*]thiazolium perchlorates, (B) pyrrolo[2,1-*b*]benzothiazolium perchlorates. (Solutions in trifluoroacetic acid. *J* values are in c./sec.)

	Proton signals									
	(A) Ring					Substituents				
Perchlorate	H-2	H-3	H-5	H-6	H-7	2-Me	3-Me	5-Me	6-Me	7-Me
(IIa)	7·93dd *J*(2, 3) 4·0 *J*(2, 6) 1·4	8·36d *J*(3, 2) 4·0	5·38m	7·76dd * *J*(6, 7) 6·3 *J*(6, 2) 1·4	7·36d * *J*(7, 6) 6·3					
(IIb)	7·74d *J*(2, 3) 4·0	8·20d *J*(3, 2) 4·0	5·23		7·00b				2·47d *J*(Me-6, H-7) = 1·4	
(IIc)	7·73d *J*(2, 3) 4·0	8·19d *J*(3, 2) 4·0	5·16						2·36 or 2·29	2·29 or 2·36
(IId)		7·91q *J*(H-3, Me-2) = 1·1	5·15		6·91q *J*(H-7, Me-6) = 1·6	2·64d *J*(Me-2 H-3) = 1·1			2·44d *J*(Me-6, H-7) = 1·6	
(IIe)	7·34q *J*(H-2, Me-3) = 1·0		5·03b		6·99q *J*(H-7, Me-6) = 1·4		2·60d *J*(Me-3, H-2) = 1·0		2·46d *J*(Me-6, H-7) = 1·4	
(IIf)	7·37b		4·99				2·60d *J*(Me-3, H-2) = 1·1		2·37 or 2·26	2·26 or 2·37
(IIg)	7·40		5·21				2·67		2·52	
(IIh)	7·78d *J*(2, 3) 4·0	8·23d *J*(3, 2) 4·0	5·70							
(IIi)		7·91q *J*(H-3, Me-2) = 1·1	5·63		7·42	2·67 *J*(Me-2, H-3) = 1·1				
(IIj)			5·43		7·34		2·63 *J*(Me-3, H-2) = 1·1			
(III)	7·80d *J*(2, 3) 4·0	8·21d *J*(3, 2) 4·0	5·21q *J*(H-5, Me-5) = 7·2					1·79d *J*(Me-5, H-5) = 7·2	2·29	2·29
(IVa)	7·79d *J*(2, 3) 4·0	8·17d *J*(3, 2) 4·0	5·21q * *J*(H-5, Me-5) = 7·3		6·95b			1·80d *J*(Me-5, H-5) = 7·3	2·39d *J*(Me-6, H-7) = 1·6	
(IVb)					4·15					

	(B) Ring						Substituent
	H-1	H-3	H-5	H-6	H-7	H-8	2-Me
(Va)	6·94q *J*(H-1, Me-2) = 1·6	4·98	2·88b	2·07b	2·07b	2·88b	2·45d *J*(Me-2, H-1) = 1·6
(Vb)	7·47	5·47	2·93b	2·10b	2·10b	2·93b	
(VI)		5·88					

Unless otherwise stated values refer to singlet absorptions. For multiplets, d = doublet, q = quartet, b = broad unresolved signal.

* Components show further weak splitting.

components of the H-2 doublet, produced by strong coupling with H-3 (*J* = 4·0 c./sec.), are each weakly split into a doublet (*J* = 1·4 c./sec.) by further long-range coupling with H-6. The components of the H-7 doublet are also weakly split owing to coupling with the 5-methylene protons. Methyl groups at positions 2, 3, or 6 are weakly coupled to the adjacent ring-proton H-3, H-2, or H-7, respectively, the corresponding signals showing the expected multiplicity (Table). A 6-methyl group is identifiable in the presence of a 2- or 3-methyl group by virtue of the difference in magnitude of the coupling constants for these interactions. The constant for the Me-6, H-7 coupling ($J = 1{\cdot}4$—$1{\cdot}6$ c./sec.) is significantly greater than that for the Me-2, H-3 or Me-3, H-2 couplings ($J = 1{\cdot}0$—$1{\cdot}1$ c./sec.).

5,6-Dimethylpyrrolo[2,1-*b*]thiazole (Ie) did not form a solid perchlorate and gave a picrate of wide melting range.[2] The spectrum of 5,6-dimethylpyrrolo[2,1-*b*]thiazole in trifluoroacetic acid shows that protonation gives a mixture of the 5H- (IVa) (85%) and the 7H-cation (IVb) (15%). It was not possible to extract the complete spectrum of compound (IVb), the signals of which in the regions of the aromatic and methyl protons are obscured by those of the 5H-form. The methylene signal of the 7H-form appears as a singlet at higher field (δ 4·15).

The chemical shifts of H-2 and H-3 in the pyrrolo[2,1-*b*]thiazolium cations are similar to those (δ 7·88 and 8·0, $J = 4{\cdot}0$ c./sec.) of the corresponding protons of 2,3-dimethylthiazolium perchlorate, showing that in the pyrrolo[2,1-*b*]thiazolium cations the thiazole ring carries the bulk of the positive charge.

EXPERIMENTAL

Melting points were determined on a Kofler heating stage. Perchloric acid refers to 70—72% w/w perchloric acid of AnalaR grade. Acetonitrile was purified by boiling it for 1 hr. over phosphoric anhydride, then distilled, and it was redistilled before use. Acetic acid was of AnalaR grade.

Proton Magnetic Resonance Spectra.—Pyrrolo[2,1-*b*]thiazoles and their perchlorates were examined as 0·4M-solutions in trifluoroacetic acid containing tetramethylsilane as internal reference. The spectra were measured at *ca.* 34° with a Perkin-Elmer R10 spectrometer operating at 60 Mc./sec., at a sweep rate of 1·6 c./sec./sec. and sweep width of 600 c./sec. Chemical shifts (δ) are given in p.p.m. downfield from the tetramethylsilane signal. *J* values were measured on the 100-c./sec. scale with an estimated accuracy of ±0·1 c./sec.

Preparation of Pyrrolo[2,1-b]*thiazolium Perchlorates.*—The majority of pyrrolo[2,1-*b*]thiazolium perchlorates were prepared according to the following general procedure. Perchloric acid (0·6 ml., 34% excess) was added to a solution of the pyrrolo[2,1-*b*]thiazole [2] (0·5 mmole) in ethanol (5 ml.) at room temperature. The solution was cooled to *ca.* 10°, and the perchlorate was filtered, washed with a small volume of ethanol followed by ether, and recrystallised from ethanol. The following salts, all forming colourless needles unless otherwise indicated, were prepared by this procedure: 6-*methyl*-5H-*pyrrolo*[2,1-b]*thiazolium perchlorate* (IIb) (97%), m. p. 122·8—123·8° (Found: C, 35·3; H, 3·3; N, 5·9; S, 13·3. $C_7H_8ClNO_4S$ requires C, 35·4; H, 3·4; N, 5·9;· S, 13·5%); 6,7-*dimethyl*-5H-*pyrrolo*[2,1-b]*thiazolium perchlorate* (IIc) (96%), m. p. 178—181° (decomp.) (Found: C, 38·3; H, 3·8; N, 5·2. $C_8H_{10}ClNO_4S$ requires C, 38·2; H, 4·3; N, 5·6%); 2,6-*dimethyl*-5H-*pyrrolo*[2,1-b]*thiazolium perchlorate* (IId) (97%), m. p. 137·5—139° (Found: C, 38·1; H, 4·5; N, 5·6; S, 12·8. $C_8H_{10}ClNO_4S$ requires C, 38·2; H, 4·3; N, 5·6; S, 12·7%); 3,6-*dimethyl*-5H-*pyrrolo*[2,1-b]*thiazolium perchlorate* (IIe) (95%), m. p. 133·5—135° (Found: C, 38·5; H, 4·0; N, 5·8. $C_8H_{10}ClNO_4S$ requires C, 38·2; H, 4·3; N, 5·6%); 3,6,7-*trimethyl*-5H-*pyrrolo*[2,1-b]*thiazolium perchlorate* (IIf) (97%), m. p. 109·5—112° (softens >105°) (Found: C, 40·7; H, 4·7; N, 5·1; S, 11·7. $C_9H_{12}ClNO_4S$ requires C, 40·7; H, 4·6; N, 5·3; S, 12·1%); 3,6-*dimethyl*-7-*phenyl*-5H-*pyrrolo*[2,1-b]*thiazolium perchlorate* (IIg) (97%), m. p. 155–157·5 (Found: C, 50·9; H, 4·7; N, 4·3; S, 10·2. $C_{14}H_{14}ClNO_4S$ requires C, 51·3; H, 4·3; N, 4·3; S, 9·9%); 5,6,7-*trimethyl*-5H-*pyrrolo*[2,1-b]*thiazolium perchlorate* (III) (94%), colourless prisms, m. p. 151—153° (softens >140°) (Found: C, 40·7; H, 4·1; N, 5·2; S, 12·5. $C_9H_{12}ClNO_4S$ requires C, 40·7; H, 4·6; N, 5·3; S, 12·1%); 5,6,7,8-*tetrahydro*-2-*methyl*-3H-*pyrrolo*[2,1-b]*benzothiazolium perchlorate* (Va) (98%), colourless plates, m. p. 137—139·5° (Found C, 45·6; H, 4·7; N, 4·7; S, 11·4. $C_{11}H_{14}ClNO_4S$ requires C, 45·3; H, 4·8; N, 4·8; S, 11·0%).

5H-*Pyrrolo*[2,1-b]*thiazolium Perchlorate* (IIa).—This *salt* was prepared according to the foregoing procedure, using methanol (5 ml.) solvent. Recrystallisation from methanol containing 1% v/v perchloric acid gave colourless needles which decomposed without melting at 200—230° (Found: N, 5·9. $C_6H_6ClNO_4S$ requires N, 6·3%).

6-*Phenyl*-5H-*pyrrolo*[2,1-b]*thiazolium Perchlorate* (IIh).—Perchloric acid (0·6 ml.) was added to a solution of 6-phenylpyrrolo[2,1-*b*]thiazole (0·5 mmole) in acetic acid (5 ml.) at 60—70°. 6-*Phenyl*-5H-*pyrrolo*[2,1-b]*thiazolium perchlorate* (88%) was obtained from the cooled solution as colourless needles, m. p. 169—171°, which decomposed upon attempted recrystallisation (Found: N, 5·1. $C_{12}H_{10}ClNO_4S$ requires N, 4·7%).

2-*Methyl*-6-*phenyl*-5H-*pyrrolo*[2,1-b]*thiazolium Perchlorate* (IIi).—Addition of perchloric acid (1·2 ml.) to a solution of 2-methyl-6-phenylpyrrolo[2,1-*b*]thiazole (1 mmole) in ethanol (40 ml.) at 65° gave 2-*methyl*-6-*phenyl*-5H-*pyrrolo*[2,1-b]*thiazolium perchlorate* (94%) as pale yellow needles, m. p. 172—175° after recrystallisation from ethanol containing 1% v/v perchloric acid (Found: N, 4·1. $C_{13}H_{12}ClNO_4S$ requires N, 4·5%).

3-*Methyl*-6-*phenyl*-5H-*pyrrolo*[2,1-b]*thiazolium Perchlorate* (IIj).—Perchloric acid (1·2 ml.) was added to a solution of 3-methyl-6-phenylpyrrolo[2,1-*b*]thiazole (1 mmole) in acetonitrile (5 ml.) at room temperature. 3-*Methyl*-6-*phenyl*-5H-*pyrrolo*[2,1-b]*thiazolium perchlorate* (93%) crystallised as colourless needles which, after recrystallisation from acetonitrile containing 1% v/v perchloric acid, had m. p. 210—216° (decomp.) (Found: N, 5·0. $C_{13}H_{12}ClNO_4S$ requires N, 4·5%).

5,6,7,8-*Tetrahydro*-2-*phenyl*-3H-*pyrrolo*[2,1-b]*benzothiazolium Perchlorate* (Vb).—Perchloric acid (1·2 ml.) was added to a solution of 5,6,7,8-tetrahydro-2-phenylpyrrolo[2,1-*b*]benzothiazole (1 mmole) in ethanol (5 ml.) at 65°. The cooled solution gave 5,6,7,8-*tetrahydro*-2-*phenyl*-3H-*pyrrolo*[2,1-b]*benzothiazolium perchlorate* (96%) which recrystallised from acetic acid as pale yellow prisms, m. p. 236—239° (decomp.) (Found: N, 3·7. $C_{16}H_{16}ClNO_4S$ requires N, 4·0%).

2-*Phenyl*-3H-*pyrrolo*[2,1-b]*benzothiazolium Perchlorate* (VI).—Perchloric acid (1·2 ml.) was added to a solution of 2-phenylpyrrolo[2,1-*b*]benzothiazole (1 mmole) in acetonitrile (5 ml.) at 65°. Addition of ether (10 ml.) to the cooled solution gave 2-*phenyl*-3H-*pyrrolo*[2,1-b]*benzothiazolium perchlorate* (99%) as pale yellow prisms, m. p. 225—228° (decomp.), which could not be recrystallised satisfactorily and were analysed without recrystallisation (Found: N, 4·2. $C_{16}H_{12}ClNO_4S$ requires N, 4·0%).

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