Reaction of Nucleophiles with Some 2-Alkylthio- and 2-Acylthio-3-alkylthiazolium Salts

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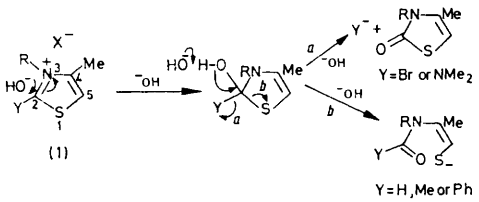
2-Alkylthio-3-alkylthiazolium salts were prepared by alkylation of either 2-alkylthiothiazoles or 3-alkyl-Δ^4-thiazoline-2-thiones; 2-acylthio-3-alkylthiazolium salts were prepared by alkylation of 2-acylthiothiazoles only. The action of a variety of nucleophiles on both species was investigated: attack took place either at C-2 of the thiazole nucleus or at the carbon atom adjacent to sulphur in the 2-substituent, depending on the nature of the nucleophile and of the 2-*S*-substituent.

A STUDY of the reaction of nucleophiles,[1,2] particularly hydroxide ion,[3] with 2-substituted 3-alkylthiazolium salts (1) established that the nature of the 2-substituent determined the reaction pathway (Scheme 1). Which pathway was followed depended on the relative abilities of Y and the ring sulphur atom as leaving groups; it thus seemed of interest to investigate species in which Y = RS, *e.g.* (2)—(7), in which there are competing $^-S^-$ leaving groups.

Preparation of NS-*Dialkyl Salts.*—The 3-alkyl-2-

[1] J. E. Downes and P. Sykes, *Chem. and Ind.*, 1959, 161.
[2] G. M. Clarke and P. Sykes, (*a*) *Chem. Comm.*, 1965, 370; (*b*) *J. Chem. Soc.* (*C*), 1967, 1411.
[3] G. M. Clarke and P. Sykes, *J. Chem. Soc.* (*C*), 1967, 1269.

alkylthiothiazolium salts (2)—(7) were obtained either by *N*-alkylation of 2-alkylthiothiazoles, *e.g.* (8) or by *S*-alkylation of 3-alkyl-Δ^4-thiazoline-2-thiones, *e.g.* (11)



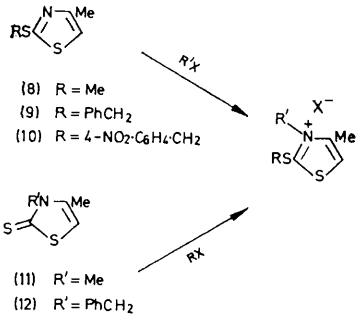
(1)

SCHEME 1

(Scheme 2). The latter route was normally preferred for making those salts in which R and R′ are different, as alkylation of 2-RS-thiazoles, *e.g.* (8), with R′X (X = I or Br) was found to lead to *NS*-(R′)$_2$ salts, *e.g.* (3), especially when an excess of R′X was used or when RX was more volatile than R′X. This alkyl exchange resulted from internal nucleophilic attack by X^- in the first-formed *N*-R′,*S*-R salt, *e.g.* (5; X = Br), to yield the *N*-R′-Δ^4-thiazoline-2-thione, *e.g.* (12), which then underwent re-alkylation by R′X to yield the *NS*-(R′)$_2$ salt, *e.g.* (3) (Scheme 3).

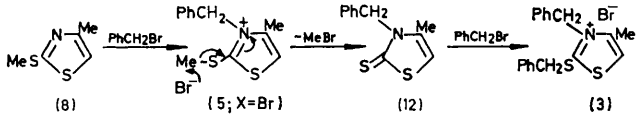
Thus treatment of (8) with 1 mol. equiv. of benzyl bromide yielded a mixture of (5; X = Br), (12), and (3), whereas use of 5 mol. equiv. resulted in almost quantitative formation of (3). That the above pathway, *i.e.* Scheme 3, was followed was borne out by the observations: (*a*) that refluxing of a solution of (2; X = I) in ethanol resulted in its partial conversion into (11), (*b*) that this conversion was speeded up, and the proportion of thione increased, by added iodide ion, and (*c*) that refluxing a solution of (2; X = I) in ethanol with benzyl bromide converted it in part into (4; X = Br). This general behaviour closely paralleled that of *NS*-dialkylthiazolinium salts,[4] except that the thiazolidine-2-thione intermediate [the analogue of (12)] did not then normally undergo *S*-alkylation. Significantly, alkyl exchange did not occur when methyl fluorosulphonate[5] was used to alkylate 2-alkylthiothiazoles, *e.g.* (9) and (10), in the preparation of (4; X = SO_3F) and (6), respectively; partly because methylation then took place under very mild conditions, but mainly because fluorosulphonate anion was such a poor 'internal nucleophile.' The latter point was borne out by the observation that heating solutions of (2; X = SO_3F) and (4; X = SO_3F) in either ethanol or xylene for several hours resulted, in contrast to (*a*), in no conversion into the thione (11).

Reactions with Nucleophiles.—The *NS*-dialkyl salt (2; X = I) was found to yield only the Δ^4-thiazolin-2-one (13) with aqueous base (Scheme 1, path *a*), whereas



	R	R′	X
(2)	Me	Me	I or SO_3F
(3)	$PhCH_2$	$PhCH_2$	Br
(4)	$PhCH_2$	Me	SO_3F or Br
(5)	Me	$PhCH_2$	I
(6)	4-NO_2·C_6H_4·CH_2	Me	SO_3F
(7)	4-NO_2·C_6H_4·CH_2	$PhCH_2$	Br

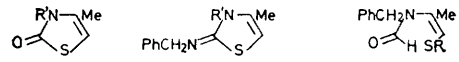
SCHEME 2



(8) (5; X=Br) (12) (3)

SCHEME 3

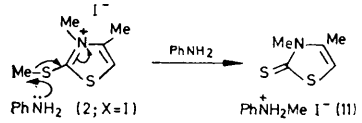
the reaction with aqueous sodium sulphide yielded the corresponding thione (11) (90%) and the thiazolinone



(13) R′ = Me
(14) R′ = $PhCH_2$
(15) R′ = Me
(16) R′ = $PhCH_2$
(17) R = $PhCH_2$
(18) R = 4-NO_2·C_6H_4·CH_2

(13) (10%), the major product arising from nucleophilic attack by ^-SH, and the minor one from competing attack by ^-OH generated in the strongly basic solution.

Benzylamine also attacked at C-2 in the nucleus to yield a mixture of the benzylimino-derivative (15) and its hydriodide, but aniline yielded the thione (11) (not the analogous phenylimino-derivative) through alternative nucleophilic attack on the carbon atom of the 2-methylthio-substituent (Scheme 4); the resultant



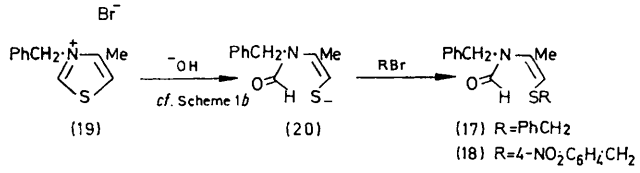
PhNH$_2$ (2; X=I) PhNH$_2$Me I$^-$ (11)

SCHEME 4

[4] A. D. Clark and P. Sykes, *J. Chem. Soc.* (*C*), 1971, 103.
[5] M. G. Ahmad, R. W. Alder, G. H. James, M. L. Sinnott, and M. C. Whiting, *Chem. Comm.*, 1968, 1533.

N-methylaniline was detected by g.l.c. A similar result was obtained with phenylhydrazine; thus its reaction and that of aniline parallel the internal nucleophilic attack by halide ion, *cf.* Scheme 3. Interestingly, the 2-methylthiothiazole (8) was recovered unchanged after heating with either benzylamine or aniline in dimethylformamide at 100° (4 h).

The behaviour of the *NS*-dibenzyl salt (3) was essentially analogous in that treatment with aqueous sodium sulphide yielded the thione (12), treatment with benzylamine yielded the benzylimino-derivative (16) (this was relatively unstable as the free base but yielded a stable hydrochloride) and a little thione (12), and treatment with aniline gave the thione (12) and *N*-benzylaniline. The reaction with aqueous base was, however, more complex: in addition to the Δ^4-thiazolin-2-one (14) (32%) and toluene-α-thiolate anion (68%; isolated as the disulphide), the thione (12) (24%; through attack at the methylene carbon atom of the 2-benzylthio-substituent) and the ring-opened product (17) (16%) were also obtained. The structure of compound (17) was confirmed by comparison with a sample obtained by *S*-benzylation (Scheme 5; R = $PhCH_2$) of the ring-opened form (20) of the thiazolium salt (19).

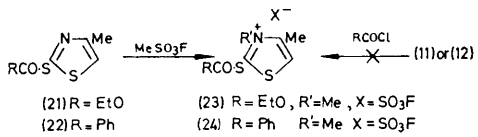


SCHEME 5

Compound (17) is different from the ring-opened product that would be obtained if the ring sulphur atom had acted as the leaving group (*b* in Scheme 1). If 4-nitrobenzyl bromide was added to the mixture of the salt (3) and aqueous base, the *S*-4-nitrobenzyl derivative (18) was obtained, in addition to (17). Compound (17) was found to be stable in the presence of aqueous base and 4-nitrobenzyl bromide; it thus seems possible that (18) is formed through *S*-4-nitrobenzylation of (20), and that it may also be formed in the base-induced cleavage of (3).

Cleavage of the salt (4; X = SO_3F) with aqueous base yielded only the thiazolinone (13) and toluene-α-thiolate anion (isolated as the disulphide), whereas (6) yielded, in addition to the above, the thione (11) (25%), reflecting the easier nucleophilic attack on the methylene carbon atom of a 2-(4-nitrobenzylthio)- as compared with a 2-benzylthio-substituent. In neither case were any ring-opened products detected.

Preparation of S-*Acyl*-N-*alkyl Salts*.—The salts (23) and (24) could be prepared only by methylation (with $MeSO_3F$) of the corresponding 2-acylthiothiazoles (21) and (22), respectively, as acyl halides were without effect on the corresponding thiones (11) and (12) (Scheme 6). This latter observation probably reflects an unfavourable equilibrium situation as acyl halides might well be expected to react with thiones, *e.g.* (11) and (12), at least as readily as do alkyl halides. It is significant in this context that a little thione remained



SCHEME 6

unalkylated unless an excess of the alkyl halide was used, *i.e.* that alkylation too involves an equilibrium situation but one that lies further in favour of products. Observation (n.m.r.) of a solution of the *NS*-dialkyl salt (3) in deuteriochloroform showed that slow dissociation to the thione (12) occurred. Equilibration was complete after *ca.* 20 h, when the ratio of (3) to (12) was *ca.* 1 : 1. Evaporation of the solution allowed almost quantitative recovery of (3), however.

Methylation of both (21) and (22) with an excess of methyl iodide yielded the *NS*-dimethyl salt (2; X = I), some starting material remaining unchanged, and benzylation of (21) with benzyl bromide yielded the *NS*-dibenzyl salt (3), some unchanged starting material, and also the *N*-benzyl thione (12). This parallels the pathway suggested (Scheme 3) for the reaction of alkyl halides with 2-alkylthiothiazoles, *e.g.* (8). The 2-acylthiothiazoles (21) and (22) were also unaffected by acyl halides, again possibly reflecting an unfavourable equilibrium situation.

Reactions with Nucleophiles.—The *S*-acyl-*N*-alkyl salt (23) reacted with benzylamine and with aniline to yield the thione (11) and ethyl *N*-benzylcarbamate or *N*-phenylcarbamate, respectively, through preferential nucleophilic attack at the carbonyl carbon atom of the 2-ethoxycarbonylthio-substituent. With hydroxide ion, however, (23) yielded the thiazolinone (13) in addition to the thione (11), in the ratio (n.m.r.) 1 : 1·6. This reflects the ability of the smaller nucleophile to effect some attack at C-2 of the thiazole nucleus. The reactions of the salt (24) followed a parallel course except that with hydroxide ion only the thione (11) (in addition to benzoic acid) was obtained, the larger phenyl group in the 2-substituent making attack at C-2 of the thiazole nucleus more difficult.

EXPERIMENTAL

M.p.s were obtained with a Reichert electrothermal apparatus. I.r. spectra were taken with a Perkin-Elmer 257 or a Unicam SP 200 instrument; n.m.r. spectra were obtained with a Perkin-Elmer R12 B or a Varian HA-100 instrument (tetramethylsilane as internal standard). T.l.c. was performed on silica gel GF 254 plates. Analytic g.l.c. was carried out with a Perkin-Elmer F11 instrument.

4-Methyl-2-(4-nitrobenzylthio)thiazole (10).—4-Methyl-Δ^4-thiazoline-2-thione [6] (9·6 g, 0·073 mol) was dissolved in dry

[6] E. R. Buchman, A. O. Reims, and H. Sargent, *J. Org. Chem.*, 1941, **6**, 764.

acetone (15 ml), and a solution of 4-nitrobenzyl bromide (17·3 g, 0·08 mol) in acetone (20 ml) and ether (20 ml) was added. The solution was set aside at room temperature for 20 h, and the pale yellow crystals which separated were washed with ether to yield the thiazole hydrobromide (23 g, 91%), m.p. 150—155°. This (15 g, 0·43 mol) was added to an excess of aqueous sodium hydroxide and the mixture extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated to yield the *thiazole* (11·4 g, 99%), m.p. 53—55° (from ethanol) (Found: C, 49·45; H, 3·95; N, 10·25. $C_{11}H_{10}N_2O_2S_2$ requires C, 49·6; H, 3·8; N, 10·5%), τ ($CDCl_3$) 7·64 (3H, s, CH_3), 5·60 (2H, s, CH_2), 3·30 (1H, s, H-5), and 1·9—2·52 (4H, d, ArH).

Preparation of NS-*Dialkyl Salts.*—(a) *By alkylation of 2-alkylthiothiazoles.* 4-Methyl-2-methylthiothiazole [6] (11 g, 0·076 mol) and methyl iodide (97 g, 0·69 mol) were heated under reflux for 48 h. The separated solid was filtered off and washed with acetone to yield *3,4-dimethyl-2-methylthiothiazolium iodide* (2; X = I) (22 g, 96%), m.p. 139—140° (from ethanol) (Found: C, 25·05; H, 3·65; N, 5·15. $C_6H_{10}INS_2$ requires C, 25·1; H, 3·5; N, 4·9%), τ [$(CD_3)_2SO$] 7·5 (3H, s, CH_3), 7·08 (3H, s, CH_3), 6·18 (3H, s, CH_3), and 2·14 (1H, s, H-5).

Treatment of 2-benzylthio-4-methylthiazole [7] in carbon tetrachloride with methyl fluorosulphonate [5] (1·1 mol) at 0° yielded *2-benzylthio-3,4-dimethylthiazolium fluorosulphonate* (4; X = SO_3F) (1·6 g, 96%), m.p. 129—131° (from ethanol) (Found: C, 43·15; H, 4·45; N, 4·2. $C_{12}H_{14}FNO_3S_3$ requires C, 42·95; H, 4·2; N, 4·2%), τ [$(CD_3)_2SO$] 7·5 (3H, s, CH_3), 6·17 (3H, s, CH_3), 5·2 (2H, s, CH_2), 2·53 (5H, m, Ph), and 2·20 (1H, s, H-5).

3,4-Dimethyl-2-methylthiothiazolium fluorosulphonate (2; X = SO_3F), m.p. 94—97°, τ [$(CD_3)_2SO$] 7·5 (3H, s, CH_3), 7·03 (3H, s, CH_3), 6·25 (3H, s, CH_3), and 2·25 (1H, s, H-5), and *3,4-dimethyl-2-(4-nitrobenzylthio)thiazolium fluorosulphonate* (6), m.p. 134—135° (from ethanol) (Found: C, 38·05; H, 3·7; N, 7·15. $C_{12}H_{13}FN_2O_5S_3$ requires C, 37·9; H, 3·45; N, 7·35%), τ [$(CD_3)_2SO$] 7·53 (3H, s, CH_3), 6·17 (3H, s, CH_3), 5·1 (2H, s, CH_2), 2·2 (1H, s, H-5), and 2·25—1·75 (4H, d, C_6H_4), were prepared similarly.

Reaction of 4-methyl-2-methylthiothiazole with benzyl bromide. Heating an equimolar mixture of 4-methyl-2-methylthiothiazole and benzyl bromide for 5 h at 110° gave a mixture containing (analysis of n.m.r. spectrum) 3-benzyl-4-methyl-2-methylthiothiazolium bromide (5; X = Br) (28%), 3-benzyl-4-methyl-Δ⁴-thiazoline-2-thione (12) (44%), and 3-benzyl-2-benzylthio-4-methylthiazolium bromide [3] (3) (28%). When an excess of benzyl bromide was employed, however, the *NS*-dibenzyl salt (3) was obtained in essentially quantitative yield.

Stability of 3,4-dimethyl-2-methylthiothiazolium salts (2 X = I *or* SO_3F). 3,4-Dimethyl-2-methylthiothiazolium iodide (0·29 g, 1 mmol) was dissolved in ethanol (4 ml) and heated under reflux for 3·5 h. Removal of the solvent under reduced pressure yielded a red solid, whose n.m.r. spectrum [in $(CD_3)_2SO$] showed the presence of unchanged starting material and 3,4-dimethyl-Δ⁴-thiazoline-2-thione [8] (11) in the ratio of 5 : 4.

Repetition of the above experiment in the presence of iodide ion [NaI (0·15 g, 1 mmol)] resulted in more rapid breakdown of the thiazolium salt, and led to a starting material (2; X = I) to thione (11) ratio of 2 : 3 after 3·5 h.

[7] J. E. Cranham, A. W. Cummings, A. M. Johnston, and H. A. Stevenson, *J. Sci. Food Agric.*, 1958, **9**, 143.

[8] J. D. Kendall and H. G. Suggate, *J. Chem. Soc.*, 1949, 1503.

3,4-Dimethyl-2-methylthiothiazolium fluorosulphonate (2; X = SO_3F) and 2-benzylthio-3,4-dimethylthiazolium fluorosulphonate (4; X = SO_3F) were both unchanged after heating for several hours in either ethanol or xylene.

Heating a solution of (2; X = I) and an excess of benzyl bromide in ethanol for 5·5 h yielded a mixture containing unchanged starting material and 2-benzylthio-3,4-dimethylthiazolium bromide (4; X = Br) in the ratio 9 : 2.

(b) *By alkylation of 3-alkyl-Δ⁴-thiazoline-2-thiones.* 3-Benzyl-4-methyl-Δ⁴-thiazoline-2-thione [9] (0·4 g, 1·8 mmol), dissolved in methyl iodide (4·5 g, 31·5 mmol), was left overnight at room temperature. The separated solid was filtered off and washed with ether to yield *3-benzyl-4-methyl-2-methylthiothiazolium iodide* (5) (0·65 g, 100%), m.p. 147—149° (from ethanol) (Found: C, 39·9; H, 3·9; N, 3·9. $C_{12}H_{14}INS_2$ requires C, 39·65; H, 3·9; N, 3·85%), τ [$(CD_3)_2SO$] 7·53 (3H, s, CH_3), 7·0 (3H, s, CH_3), 4·4 (2H, s, CH_2), 2·65 (5H, m, Ph), and 2·08 (1H, s, H-5).

2-Benzylthio-3,4-dimethylthiazolium bromide (4; X = Br), m.p. 135—158° (Found: C, 45·7; H, 4·65; N, 4·2. $C_{12}H_{14}BrNS_2$ requires C, 45·55; H, 4·45; N, 4·45%), τ [$(CD_3)_2SO$] 7·53 (3H, s, CH_3), 6·20 (3H, s, CH_3), 5·23 (2H, s, CH_2), 2·60 (5H, m, Ph), and 2·2 (1H, s, H-5); 3,4-dimethyl-2-methylthiothiazolium iodide (2; X = I), m.p. 140—142°; 3-benzyl-2-benzylthio-4-methylthiazolium bromide [3] (3), m.p. 83—86° (from ethanol–ether), τ ($CDCl_3$) 7·5 (3H, s, CH_3), 5·35 (2H, s, CH_2), 4·28 (2H, s, CH_2), 2·65 (10H, m, 2 × Ph), and 1·75 (1H, s, H-5); and *3-benzyl-2-(4-nitrobenzylthio)thiazolium bromide* (7), m.p. 119° (Found: C, 49·3; H, 3·85; N, 6·5. $C_{18}H_{17}BrN_2O_2S_2$ requires C, 49·45; H, 3·9; N, 6·4%), τ [$(CD_3)_2SO$] 7·55 (3H, s, CH_3), 5·0 (2H, s, CH_2), 4·35 (2H, s, CH_2), 2·68 (5H, m, Ph), 2·25—1·77 (4H, d, ArH), and 2·0 (1H, s, H-5), were prepared similarly.

Reversibility of thione alkylation. After treatment of the 3-alkyl-Δ⁴-thiazoline-2-thiones with an equimolar proportion of an alkyl halide, small amounts of thione (9—25%) were always recovered in addition to the thiazolium salt. Use of an excess of alkyl halide (several mol. equiv.) drove the apparent equilibrium almost to completion, however.

The n.m.r. spectrum of 3-benzyl-2-benzylthio-4-methylthiazolium bromide (3) in deuteriochloroform demonstrated its slow dissociation into 3-benzyl-4-methyl-Δ⁴-thiazoline-2-thione (12). This was complete after 20 h, when (3) was *ca.* 50% dissociated; on allowing the solvent to evaporate, however, almost 100% of the original (3) could be recovered.

3-Benzyl-4-methyl-Δ⁴-thiazolin-2-one (14).—Benzylamine (10·7 g, 0·1 mol) in ethanol (15 ml) was treated with a stream of carbon oxysulphide [generated from saturated ammonium thiocyanate (25 ml) and concentrated sulphuric acid (150 ml)].[10] The separated solid was filtered off and washed with ether to yield the benzylamine salt of *N*-benzylthiocarbamic acid (4·5 g, 33%).

The salt (2·5 g, 9·2 mmol) was suspended in methanol (60 ml) and chloroacetone (1·04 g, 11 mmol) was added. The mixture was set aside for 1 h at room temperature, and then refluxed with dilute hydrochloric acid (6 ml) for 20 min. The solvent was removed under reduced pressure and the residue extracted with ether. The extract was

[9] A. Rieche, G. Hilgetag, D. Martin, and L. Kreyzi, *Arch. Pharm.*, 1963, **296**, 310.

[10] G. Brauer (ed.), ' Handbuch der Präparitiven Anorganischen Chemie,' I Band, Ferdinand Enke Verlag, Stuttgart, 1960, p. 580.

washed with water, dried (Na_2SO_4), and evaporated to yield the thiazolinone (1·1 g, 63%), m.p. 74·5—75·5° (from cyclohexane) (lit.,[11] 74—75°) (Found: C, 64·6; H, 5·2; N, 6·65. Calc. for $C_{11}H_{11}NOS$: C, 64·4; H, 5·2; N, 6·8%), $\nu_{max.}$ (Nujol) 1625 cm^{-1} (C=O), τ ($CDCl_3$) 8·0 (3H, s, CH_3), 5·1 (2H, s, CH_2), 4·30 (1H, s, H-5), and 2·8 (5H, s, Ph).

Similar treatment of methylamine yielded 3,4-dimethyl-Δ^4-thiazolin-2-one (13), m.p. 45—47·5° (lit.,[12] 48—49°) (Found: C, 46·25; H, 5·65; N, 10·9. Calc. for C_5H_7NOS: C, 46·5; H, 5·45; N, 10·85%), $\nu_{max.}$ (Nujol) 1680—1620 cm^{-1} (C=O), τ ($CDCl_3$) 7·9 (3H, s, CH_3), 6·75 (3H, s, CH_3N), and 4·27 (1H, s, H-5).

Action of Nucleophiles on NS-*Dialkyl Salts.*—(a) *Sodium sulphide.* (i) 3,4-*Dimethyl*-2-*methylthiothiazolium iodide* (2; X = I). The salt (2·87 g, 0·01 mol) was dissolved in water (4 ml) and sodium sulphide (4·8 g, 0·02 mol) in water (10 ml) was added. The solid which immediately separated was filtered off and washed with water to yield 3,4-dimethyl-Δ^4-thiazoline-2-thione (11) (1·28 g, 88%), m.p. 114° (from ethanol) (lit.,[8] 119°) (Found: C, 41·55; H, 4·95; N, 9·55. Calc. for $C_5H_7NS_2$: C, 41·35; H, 4·85; N, 9·65%), τ ($CDCl_3$) 7·7 (3H, s, CH_3), 6·35 (3H, s, CH_3), and 3·75 (1H, s, H-5).

The residual aqueous solution was extracted with methylene chloride. The extract was washed with water, dried (Na_2SO_4), and evaporated to yield 3,4-dimethyl-Δ^4-thiazolin-2-one [12] (13) (0·17 g, 13%), identical (n.m.r. spectrum) with authentic material.

(ii) 3-*Benzyl*-2-*benzylthio*-4-*methylthiazolium bromide* (3). Similar treatment of this salt (in aqueous dimethylformamide), followed by chromatographic separation on silica gel yielded dibenzyl disulphide (97%), m.p. 67—69° (lit.,[13] 69—70°), and 3-benzyl-4-methyl-Δ^4-thiazoline-2-thione (12) (82%), m.p. 88·5—89·5° (from ethanol) (lit.,[9] 89°), identical (n.m.r. spectrum) with authentic material (Found: C, 59·7; H, 5·3; N, 6·3. Calc. for $C_{11}H_{11}NS_2$: C, 59·7; H, 5·0; N, 6·35%).

(b) *Benzylamine.* (i) 3-*Benzyl*-2-*benzylthio*-4-*methylthiazolium bromide* (3). The salt (2·05 g, 5 mmol) was dissolved in warm methylene chloride (30 ml) and benzylamine (1·07 g, 10 mmol) was added. The solution was stirred for 40 min and then evaporated under reduced pressure. The residue was stirred in ether (75 ml) and benzylamine hydrobromide was filtered off. The ethereal solution was evaporated to yield a pale yellow oil which on t.l.c. showed three spots. The mixture was separated by column chromatography on silica gel: elution with methylene chloride yielded dibenzyl disulphide (0·57 g, 93%) and 3-benzyl-4-methyl-Δ^4-thiazoline-2-thione (12) (0·17 g, 15%), identical (n.m.r. and t.l.c.) with authentic material. Continued elution with 20% ethyl acetate in methylene chloride yielded 3-benzyl-2-benzylimino-4-methyl-Δ^4-thiazoline (16) (0·95 g, 71%), identical (n.m.r. and i.r.) with authentic material.

A portion was dissolved in ether and the solution was saturated with hydrogen chloride gas. The separated gum was crystallised from ethanol–ether to yield the thiazoline (16) hydrochloride, m.p. 198—201°, identical (n.m.r.) with authentic material (Found: C, 65·15; H, 5·8; N, 8·6. Calc. for $C_{18}H_{19}ClN_2S$: C, 65·35; H, 5·8; N, 8·45%) prepared as follows.

NN'-Dibenzylthiourea [14] (1·3 g, 5 mmol) was dissolved with warming in toluene (15 ml) and chloroacetone (0·46 g, 5 mmol) was added at 95°. The solution was heated under reflux for 1 h, and on cooling the *benzyliminothiazoline* (16) *hydrochloride* separated (1·5 g, 95%), m.p. 200—202° (from ethanol–ether) (Found: C, 65·6; H, 5·95; N, 8·65. $C_{18}H_{19}ClN_2S$ requires C, 65·35; H, 5·8; N, 8·45%), τ [$(CD_3)_2SO$] 7·8 (3H, s, CH_3), 5·43 (2H, s, CH_2), 4·38 (2H, s, CH_2), 3·15 (1H, s, H-5), 2·68 (10H, s, 2 × Ph), and −1·2br (1H, s, ^+NH).

Treatment of the hydrochloride with aqueous base yielded the thiazoline (16) as an oil (1·02 g, 94%), τ ($CDCl_3$) 8·03 (3H, s, CH_3), 5·68 (2H, s, CH_2), 4·93 (2H, s, CH_2), 4·5 (1H, s, H-5), and 2·75 (10H, s, 2 × Ph). The free base underwent some decomposition at room temperature overnight (t.l.c.).

(ii) 3,4-*Dimethyl*-2-*methylthiothiazolium iodide* (2; X = I). Similar treatment of this salt (in dimethylformamide) yielded 2-*benzylimino*-3,4-*dimethyl*-Δ^4-*thiazoline hydriodide* (3 g, 87%), m.p. 211—213° (from ethanol) (Found: C, 41·2; H, 4·4; N, 8·65. $C_{12}H_{15}IN_2S$ requires C, 41·6; H, 4·4; N, 8·1%), τ [$CDCl_3$–$(CD_3)_2SO$] 7·7 (3H, s, CH_3), 6·27 (3H, s, CH_3), 5·45 (2H, s, CH_2), 3·35 (1H, s, H-5), and 2·62 (5H, m, Ph). An oil was also obtained which n.m.r. spectroscopy showed to be a mixture of 2-benzylimino-3,4-dimethyl-Δ^4-thiazoline, benzylamine, and dimethylformamide.

Treatment of the thiazoline hydriodide with aqueous base yielded the free *benzyliminothiazoline*, m.p. 66—67° (Found: C, 66·0; H, 6·65; N, 12·75. $C_{12}H_{14}N_2S$ requires C, 66·0; H, 6·45; N, 12·85%), $\nu_{max.}$ (Nujol) 1625 cm^{-1} (C=N), τ ($CDCl_3$) 7·9 (3H, s, CH_3), 6·7 (3H, s, CH_3), 5·7 (2H, s, CH_2), 4·5 (1H, s, H-5), and 2·7 (5H, m, Ph).

(iii) 4-*Methyl*-2-*methylthiothiazole* (8).—The 2-methylthiothiazole was recovered unchanged after 4 h at 100° with benzylamine in dimethylformamide.

(c) *Aniline.* (i) 3,4-*Dimethyl*-2-*methylthiothiazolium iodide* (2; X = I).—The salt (1·44 g, 5 mmol) and aniline (0·93 g, 10 mmol) were dissolved in dimethylformamide (5 ml) and heated at 90° for 4·5 h. G.l.c. of the resultant solution (5 ft × 1/8 in Pennwalt 223 amine packing plus 4% KOH on 85—100 mesh Gaschrom R; oven temperature 160°) showed the presence of aniline and *N*-methylaniline (t_R 10·3 and 14·7 min, respectively; identical with those of authentic materials) and 3,4-dimethyl-Δ^4-thiazoline-2-thione (11) (also detected on t.l.c.). The solution was evaporated (<40° at 0·1 mmHg) and extracted with ether. Removal of solvent under reduced pressure, and crystallisation of the residue from ethanol, yielded the thione (0·6 g, 83%), m.p. 113—114°, identical (n.m.r.) with authentic material.

(ii) 3-*Benzyl*-2-*benzylthio*-4-*methylthiazolium bromide* (3). Similar treatment of this salt yielded 3-benzyl-4-methyl-Δ^4-thiazoline-2-thione (12) and *N*-benzylaniline, τ ($CDCl_3$) 6·35br (1H, s, NH), 5·75 (2H, s, CH_2), 3·4—2·9 (5H, m, Ph), and 2·7 (5H, s, Ph).

(iii) 4-*Methyl*-2-*methylthiothiazole* (8). The thiazole was recovered unchanged after being heated with aniline in dimethylformamide at 100° for 4 h.

(d) *Phenylhydrazine.* 3,4-*Dimethyl*-2-*methylthiothiazolium iodide* (2; X = I). The salt (0·9 g, 3·1 mmol), on heating with phenylhydrazine (0·67 g, 6·2 mmol) in dimethylformamide (2 ml) at 105° for 2 h, was converted almost entirely (t.l.c. and n.m.r.) into 3,4-dimethyl-Δ^4-thiazoline-2-thione (11).

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(e) *Hydroxide ion.* (i) 3,4-*Dimethyl*-2-*methylthiothiazolium iodide* (2; X = I). The salt (4·31 g, 0·015 mol) was dissolved in water (5 ml) and sodium hydroxide solution (4N; 7·5 ml, 0·03 mol) was added. The solution was stirred for 10 min and then evaporated (<40° at 0·1 mmHg). The residue was extracted with ether and the extract was washed with water, dried (Na_2SO_4), and evaporated to yield 3,4-dimethyl-Δ^4-thiazolin-2-one (13) (1·8 g, 94%), m.p. 46·5—48°, identical (n.m.r. and i.r.) with authentic material.

(ii) 3-*Benzyl*-2-*benzylthio*-4-*methylthiazolium bromide* (3). (*a*) The salt (2·05 g, 5 mmol) was suspended in warm water (75 ml) and sodium hydroxide solution (4N; 2·5 ml, 10 mmol) was added. After stirring for 40 min a gum separated, and iodine (0·64 g, 2·5 mmol) dissolved in sodium iodide solution (20%; 10 ml) was added. The mixture was stirred for 1 h and the resultant orange gum was extracted into ether. The extract was washed with water, dried (Na_2SO_4), and evaporated to yield a dark red gum, t.l.c. of which showed 4 major spots. The mixture was separated by preparative t.l.c. (silica gel; 6% acetonitrile in benzene) to yield dibenzyl disulphide (0·42 g, 68%), 3-benzyl-4-methyl-Δ^4-thiazoline-2-thione (12) (0·26 g, 23%), 3-benzyl-4-methyl-Δ^4-thiazolin-2-one (14) (0·32 g, 31%), and *N*-benzyl-*N*-(2-benzylthio-1-methylvinyl)formamide (17) (0·23 g, 16%) (see below). The n.m.r. and i.r. spectra of these isolated materials were identical with those of authentic samples.

(*b*) Repetition in dimethylformamide under nitrogen, followed by addition of 4-nitrobenzyl bromide (1 mol. equiv.) in dimethylformamide, and separation by preparative t.l.c. (silica gel; 6% acetonitrile in benzene) yielded dibenzyl disulphide (0·42 g, 68%), 4-nitrobenzyl benzyl sulphide (0·1 g, 7%), the thione (12) (0·26 g, 24%), the thiazolinone (14) (0·34 g, 33%), the *N*-benzylformamide derivative (17) (0·22 g, 15%), and *N*-benzyl-*N*-[2-(4-nitrobenzylthio)-1-methylvinyl]formamide (18) (0·18 g, 10%), m.p. 97—100° (lit.,[15] 104°), identical (n.m.r. and i.r.) with authentic material. The *N*-benzylformamide (17) was unchanged when treated with sodium hydroxide solution followed by 4-nitrobenzyl bromide (equimolar portions). An authentic sample was prepared as follows.

3-Benzyl-4-methylthiazolium bromide (2·05 g, 7·5 mmol) was dissolved in methanol (10 ml) and water (4 ml), and aqueous sodium hydroxide (4N; 3·75 ml, 15 mmol) was then added, the solution being kept under nitrogen. After 2 min benzyl bromide (1·28 g, 7·5 mmol) was added, and the mixture stirred for 10 min. The solvent was removed and the residue extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated to yield the S-*benzyl derivative* (17) as a reddish oil (2·2 g, 100%). A portion was purified by preparative t.l.c. on silica gel with 7% acetonitrile in benzene (Found: C, 72·85; H, 6·6; N, 4·7; S, 10·75. $C_{18}H_{19}NOS$ requires C, 72·7; H, 6·45; N, 4·7; S, 10·75%), $\nu_{max.}$ (film) 1675 cm^{-1} (C=O), τ ($CDCl_3$) 8·25 (3H, s, CH_3), 6·3 (2H, s, CH_2S), 5·35 (2H, s, CH_2N), 4·3 (1H, s, H-2), 2·75 (5H, s, Ph), and 1·9 (1H, s, NCHO).

(iii) 2-*Benzylthio*-3,4-*dimethylthiazolium fluorosulphonate* (4; X = SO_3F). Similar treatment of this salt yielded dibenzyl disulphide and 3,4-dimethyl-Δ^4-thiazolin-2-one (13) (81%).

(iv) 3,4-*Dimethyl*-2-(4-*nitrobenzylthio*)*thiazolium fluorosulphonate* (6). Similar treatment of this salt yielded bis-4-nitrobenzyl disulphide[16] (60%), the thiazolin-2-one (13) (54%), and 3,4-dimethyl-Δ^4-thiazoline-2-thione (11) (25%).

2-*Benzoylthio*-4-*methylthiazole* (22).—4-Methyl-Δ^4-thiazoline-2-thione (2·8 g, 0·021 mol) was dissolved in a solution of sodium ethoxide [from sodium (0·5 g, 0·022 mol) in dry ethanol (20 ml)] and the ethanol was then removed under reduced pressure. The resultant sodium salt was suspended in dry benzene (30 ml), and benzoyl chloride (3 g, 0·021 mol) was added. The mixture was heated under reflux for 1 h, and the separated sodium chloride was then filtered off. The solvent was removed under reduced pressure to yield the *thiazole* (4 g, 80%), m.p. 60—61° (from hexane) (Found: C, 55·85; H, 3·85; N, 6·05. $C_{11}H_9NOS_2$ requires C, 56·15; H, 3·85; N, 5·95%), $\nu_{max.}$ (Nujol) 1665 cm^{-1} (C=O), τ ($CDCl_3$) 7·5 (3H, s, CH_3), 2·9 (1H, s, H-5), and 2·0—2·44 (5H, m, Ph).

2-*Ethoxycarbonylthio*-3,4-*dimethylthiazolium fluorosulphonate* (23).—2-Ethoxycarbonylthio-4-methylthiazole[6] (2·5 g, 0·012 mol) was dissolved in dry carbon tetrachloride (10 ml) and cooled to 0°; methyl fluorosulphonate (2 g, 0·017 mol) was then added. The mixture was stirred at 0° for 30 min and then at room temperature for 1 h. The solvent was decanted off and the residue dried under vacuum to yield the *thiazolium salt* as a hygroscopic oil (3·77 g, 99%) (Found: C, 28·75; H, 4·0; N, 4·2. $C_{18}H_{12}FNO_5S_3,H_2O$ requires C, 28·65; H, 4·2; N, 4·2%), $\nu_{max.}$ (film) 1740 cm^{-1} (C=O), τ [$(CD_3)_2CO$] 8·6 (3H, t, *J* 12·5 Hz, CH_3), 7·25 (3H, s, CH_3), 5·77 (3H, s, CH_3), 5·43 (2H, q, *J* 12·5 Hz, CH_3), and 1·67 (1H, s, H-5).

2-*Benzoylthio*-3,4-*dimethylthiazolium fluorosulphonate* (24), m.p. 68—97° (decomp.) (Found: C, 39·5; H, 3·7; N, 3·6. $C_{12}H_{12}FNO_4S_3,H_2O$ requires C, 39·2; H, 3·85; N, 3·8%), τ [$(CD_3)_2CO$] 7·23 (3H, s, CH_3), 5·75 (3H, s, CH_3), 2·23—1·83 (5H, m, Ph), and 1·7 (1H, s, H-5), was prepared similarly.

Other Attempted Alkylations/Acylations.—When kept overnight in an excess of methyl iodide the 2-acylthiothiazoles (21) and (22) were each converted into a mixture of 3,4-dimethyl-2-methylthiothiazolium iodide (2; X = I) and unchanged thiazole: no 3-methyl-2-acylthiothiazolium salts were obtained. Heating compound (22) with an equimolar proportion of benzyl bromide for 3 h at 100° yielded a mixture of the *NS*-dibenzylthiazolium bromide (3), the *N*-benzyl thione (12), and some unchanged (22).

Both ethyl chloroformate and benzoyl chloride were without effect on the thiones (11) and (12), the 2-acylthiothiazoles (21) and (22), and the 2-alkylthiothiazole (8).

Action of Nucleophiles on S-*Acyl*-N-*alkyl Salts.* (a) *Benzylamine.* (i) 2-*Benzoylthio*-3,4-*dimethylthiazolium fluorosulphonate* (24). The salt (1·75 g, 5 mmol) was dissolved in acetone (30 ml) and benzylamine (1·07 g, 10 mmol) was added. The mixture was stirred for 30 min, the solvent removed under reduced pressure, and the residue added to a mixture of methylene chloride and water. The methylene chloride layer was separated, washed with water, and evaporated to yield a pale yellow solid. Chromatography on silica gel yielded 3,4-dimethyl-Δ^4-thiazoline-2-thione (11) (0·68 g, 95%), m.p. 113—114°, identical (n.m.r.) with authentic material, and *N*-benzylbenzamide (0·95 g, 90%), m.p. 105—107° (lit.,[17] 104—107°), τ ($CDCl_3$) 5·45 (2H, d, *J* 10 Hz, CH_2), 3·4br (1H, s, NH), and 2·7—2·25 (10H, m, 2 × Ph).

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(ii) 2-*Ethoxycarbonylthio*-3,4-*dimethylthiazolium fluorosulphonate* (23). Similar treatment of this salt yielded the thione (11) and ethyl *N*-benzylcarbamate as an oil (lit.,[18] m.p. 47—48°) (Found: C, 67·15; H, 7·35; N, 7·85. Calc. for $C_{10}H_{13}NO_2$: C, 67·0; H, 7·3; N, 7·8%), $\nu_{max.}$ (film) 1720 cm^{-1} (C=O), τ ($CDCl_3$) 8·77 (3H, t, *J* 12·5 Hz, CH_3), 5·82 (2H, q, *J* 12·5 Hz, CH_2), 5·63 (2H, d, *J* 10 Hz, CH_2), 5·05br (1H, s, NH), and 2·73 (5H, s, Ph).

(b) *Aniline.* (i) 2-*Ethoxycarbonylthio*-3,4-*dimethylthiazolium fluorosulphonate* (23). The salt (3·35 g, 0·01 mol) was dissolved in acetone (9 ml) and aniline (1·86 g, 0·02 mol) was added. The solution was stirred for 2 h and then evaporated. The residue was extracted with methylene chloride, washed with water, and evaporated to yield a pale brown solid. Chromatography on silica gel with ethyl acetate–cyclohexane as eluant yielded 3,4-dimethyl-Δ^4-thiazoline-2-thione (11) (1·4 g, 97%), m.p. 113—115°, identical (n.m.r.) with authentic material, and ethyl carbanilate (1·6 g, 97%), m.p. 49—51° (lit.,[19] 53°), τ ($CDCl_3$) 8·7 (3H, t, *J* 12·5 Hz, CH_3), 5·8 (2H, q, *J* 12·5 Hz, CH_2), and 2·65 (5H, m, Ph).

(ii) 2-*Benzoylthio*-3,4-*dimethylthiazolium fluorosulphonate* (24). Similar treatment of this salt yielded the thione (11) and benzanilide, m.p. 162° (lit.,[20] 163°).

(c) *Hydroxide ion.* (i) 2-*Ethoxycarbonylthio*-3,4-*dimethylthiazolium fluorosulphonate* (23). The salt (1·46 g, 4·5 mmol) was dissolved in acetone (5 ml) and aqueous sodium hydroxide (4N; 2·25 ml, 9 mmol) was added. Heat was evolved and the solid ($NaFSO_3$) that separated was filtered off. The solution was concentrated under reduced pressure, and the residue dissolved in methylene chloride. This extract was washed with water, dried (Na_2SO_4), and evaporated to yield a pale yellow solid. T.l.c. and n.m.r. spectroscopy showed the presence of 3,4-dimethyl-Δ^4-thiazoline-2-thione (11) and 3,4-dimethyl-Δ^4-thiazolin-2-one (13) in the ratio 1·6 : 1. The mixture was separated by preparative t.l.c. (silica gel in methylene chloride) to yield the thione (0·37 g, 57%), m.p. 112—113°, and the thiazolinone (0·15 g, 26%), m.p. 42—46°, identical (n.m.r. and i.r.) with authentic material.

(ii) 2-*Benzoylthio*-3,4-*dimethylthiazolium fluorosulphonate* (24). Similar treatment of this salt yielded the thione (11) (96%) and benzoic acid, m.p. 123° (lit.,[21] 121°).

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