Cyclization of *N*-Formyl- and *N*-Thioformyl-sarcosine-*N*-methylthioamide into Methylaminothiazolium and *anhydro*-Mercaptoimidazolium Hydroxide Derivatives

By **Mikael Begtrup**, Department of Organic Chemistry, The Technical University of Denmark, DK–2800 Lyngby, Denmark

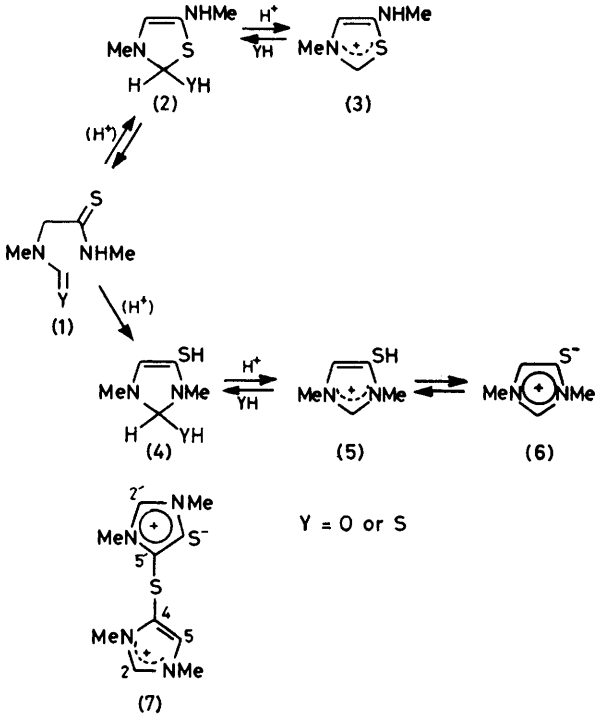
N-Formylsarcosine-*N*-methylthioamide is transformed into 1,3-dimethyl-4-mercaptoimidazolium ion on treatment with trifluoroacetic acid in acetonitrile, while the thioformyl analogue produces 3-methyl-5-methylaminothiazolium ion under the same conditions. The latter ion rearranges irreversibly to the former in aqueous acid or, in base, to its deprotonated derivative, *anhydro*-1,3-dimethyl-4-mercaptoimidazolium hydroxide. Aqueous base deformylates *N*-formylsarcosine-*N*-methylthioamide, while aqueous or non-aqueous bases convert the thioformyl analogue into *anhydro*-1,3-dimethyl-4-mercaptoimidazolium hydroxide. *N*-Formyl- and *N*-thioformyl-sarcosine-*N*-methylthioamide yield 3-methyl-5-acylmethylaminothiazolium salts when treated with acetyl chloride or trifluoroacetic anhydride. The trifluoracetylaminothiazolium salt is readily deacylated. Mechanisms are elucidated by means of deuterium exchange experiments. The reaction of 5-methylthiothiazolium salts with amines has been rationalized.

THE few known *anhydro*-1,3-disubstituted 4-mercaptoimidazolium hydroxides [parent compound (6)] have been prepared *via* 1,3-dipolar cycloaddition of phenyl isothiocyanate to 3-substituted *anhydro*-5-hydroxyoxazolium[1] or thiazolium hydroxides,[2] by treatment of 3-substituted 5-methylthiothiazolium salts with primary aliphatic amines,[3,4] or by heating *NN'*-disubstituted glycinethioamides with triethyl orthoformate or *N*-phenylbenzimidoyl chloride.[5] Two alternative potential routes were of no avail, (*i*) selective *S*-dealkylation of 1,3-disubstituted 4-methylthioimidazolium salts,[6] and (*ii*) replacement of halogen in 1,3-disubstituted 4-halogenoimidazolium salts with sulphide ions.[6] The latter reaction leads to ring-opening and formation of *N*-acyl-*N*-alkylglycine-*N'*-alkylthioamides [parent compound (1)]. These, and their thioacyl analogues have now been shown to function as suitable precursors for both *anhydro*-4-mercaptoimidazolium hydroxides and 3-substituted 5-alkylaminothiazolium salts [parent compound (3)].

RESULTS AND DISCUSSION

Thus, *N*-formylsarcosine-*N*-methylthioamide (1; Y = O) on treatment with trifluoroacetic acid, according to ^{1}H n.m.r. spectra, cyclizes to yield a 1 : 1 mixture of 3-methyl-5-methylaminothiazolium ion (3) and 1,3-dimethyl-4-mercaptoimidazolium ion (5). A slightly different ratio (1 : 1.4) is obtained from the faster reacting *N*-thioformylsarcosine-*N*-methylthioamide (1; Y = S). Since both products are stable under the reaction conditions, the composition is kinetically determined. No intermediates could be detected by ^{1}H n.m.r. spectroscopy, suggesting that the cyclization steps (Scheme 1) are the rate-limiting processes. The mercaptoimidazolium ion is stable also in dilute aqueous acid, whereas the aminothiazolium ion reconverts to *N*-formylsarcosine *N*-methylthioamide (1), most likely *via* (2). Cyclization and equilibration to (5) can therefore be accomplished in a single step by a 5-min reflux of (1) in 70% aqueous trifluoroacetic acid. In more dilute acid hydrolysis to sarcosine-*N*-methylthioamide (8) competes with the cyclization reaction.

Cyclization of (1; Y = O or S) in dry acetonitrile, containing 1 equiv. trifluoroacetic acid, provides a convenient route to either (3) or (5). Thus, *N*-thioformylsarcosine-*N*-methylthioamide (1; Y = S) affords methylaminothiazolium ion (3) as the sole product, whereas the



SCHEME 1

N-formyl derivative (1; Y = O) preponderantly produces mercaptoimidazolium ion (5), the thermodynamically more stable product; the water required for the equilibration arises through the aromatization step.

^{1}H N.m.r. data (Table 1) indicate that the aminothiazolium ion adopts structure (3) in acidic solution.

H-4 is however exchanged with deuterium in non-aqueous deuteriotrifluoroacetic acid, demonstrating that protonation at C-4 is significant. Under similar conditions, H-5 of the mercaptoimidazolium ion (5) does not undergo exchange, concordant with the fact that enethiols are weaker bases than enamines. Exchange of H-5 of (5) is observed, however, in aqueous acid even when the position of the various signals is virtually acid-independent. *N*-Formylsarcosine-*N*-methylthioamide (1) is not involved in the exchange process since its methylene protons are not deuteriated in acidic solution. Most likely, water attacks C-2 of (5) with formation of the neutral adduct (4; Y = O), a better proton acceptor than its positively charged precursor (5). Hence, the sole non-reversible step is the ring closure of (1; Y = O or S) to (4; Y = O or S).

The mercaptoimidazolium ion (5) is readily deprotonated; H-2, but not H-5, is deuteriated in neutral D_2O oxide (6). Most likely, the amine acts as the catalyst, YH, in the sequences shown in Scheme 1. Aqueous base converts the aminothiazolium ion (3) into *anhydro*-mercaptoimidazolium hydroxide (6) and *N*-formyl-sarcosine-*N*-methylthioamide (1), which undergoes further hydrolysis to sarcosine-*N*-methylthioamide (8). Most likely, (1) arises *via* (2). ^1H N.m.r. signals, attributable to (2), are observed if the pH is maintained at 7—8. Attempts to isolate (2) were unsuccessful. While aqueous base leads to extensive deformylation of *N*-formylsarcosine-*N*-methylthioamide (1), and non-aqueous base (triethylamine) leaves it unchanged, the thioformyl analogue is converted quantitatively into *anhydro*-1,3-dimethyl-4-mercaptoimidazolium hydroxide (6) by 1N aqueous sodium hydroxide or by triethylamine in acetonitrile. Most likely, this cyclization is initiated by abstraction of the thioamide proton, readily exchangeable in neutral D_2O (Scheme 2).

TABLE 1

Hydrogen-1 n.m.r. chemical shifts (p.p.m.) and coupling constants (Hz) of mercaptoimidazolium and aminothiazolium derivatives

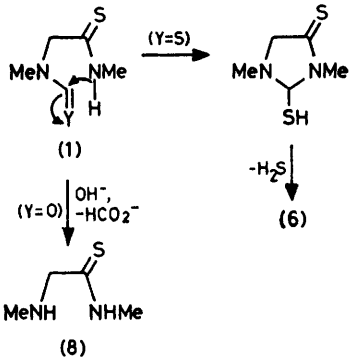
Compound	Solvent	H-2	H-5	$J_{H-2,H-5}$	*endo*-NMe	*exo*-NMe	CMe
(5) [c]	*a*	9.04	7.67	1.8	3.95 3.91		
(6)	*a*	8.36	6.82	1.0	3.75 3.65		
(12; R = MeCO) [d]	*a*	9.03	7.80	2.0	3.98 3.80		2.58
(14; R = CF_3CO) [c]	*b*	8.77	7.75		3.89 3.80		
			H-4	$J_{H-2,H-4}$			
(3) [c]	*a*	8.85	7.16	1.8	4.06	2.87	
(11; R = MeCO) [d]	*a*	9.40	8.11	1.8	4.22	3.60	2.47
(11; R = CF_3CO) [c]	*a*	9.74	8.49	1.6	4.35	3.82 ($J_{H,F}$ 1.0)	
(2) [c]	*a*	9.05	7.52	1.9	4.13	3.30	

[a] In D_2O relative to DSS. [b] In CD_3CN relative to $SiMe_4$. [c] As the trifluoroacetate. [d] As the chloride.

like H-2 of other imidazolium salts.[7] Strong bases, like sodium hydroxide, convert (5) into *anhydro*-1,3-dimethyl-4-mercaptoimidazolium hydroxide (6) whereas bases of decreasing strength produce increasing amounts of *anhydro*-1,3-dimethyl-5-(1,3-dimethylimidazolium-4-thio)-4-mercaptoimidazolium hydroxide (7) * as a by-product. Thus, sodium hydrogencarbonate yields a 1 : 7 mixture of (6) and (7), 2,6-dimethylpyridine yields exclusively (7), while weaker bases, *e.g.* pyridine, do not deprotonate the starting material extensively.

H-2, but not H-4, of the aminothiazolium ion (3) is deuteriated in neutral D_2O, a feature characteristic of thiazolium salts.[7] Non-aqueous propylamine smoothly converts (3) into *anhydro*-mercaptoimidazolium hydr-

Acetyl chloride or trifluoroacetic anhydride effect cyclization of *N*-formyl- or *N*-thioformyl-sarcosine-*N*-methylthioamide (1; Y = O or S) to give exclusively

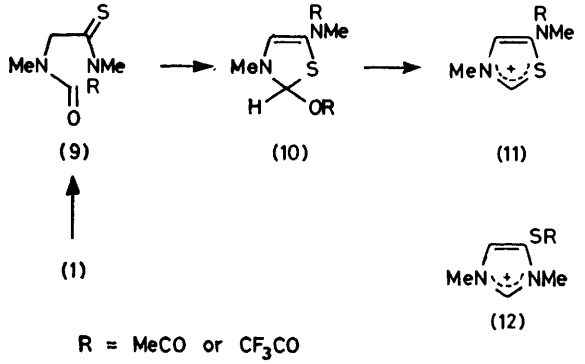


SCHEME 2

the 5-acetyl- or 5-trifluoroacetyl-methylamino-3-methylthiazolium ions (11; R = MeCO or CF_3CO). The same compounds arise by acylation of the aminothiazolium ion (3). Similarly, the mercaptoimidazolium ion (5) can be acylated to (12; R = MeCO or CF_3CO). In com-

* The *anhydro*-imidazoliumthio-mercaptoimidazolium hydroxide (7) was identified through its mass spectrum and its ^1H and ^{13}C n.m.r. spectra which exhibit chemical shifts, ^1H–^1H and ^{13}C–^1H coupling constants, and ring-proton exchange rates similar to those of the imidazolium ions (5) and (6), but distinctly different from those of the aminothiazolium ion (3) (see Experimental section). Most likely, (7) arises from attack of *anhydro*-mercaptoimidazolium hydroxide (6) at C-5 of the corresponding acid (5). The nature of the subsequent oxidation remains obscure. Acids convert (7) into its precursor (5), while strong bases cause its decomposition.

petitive experiments, (5) is acylated more easily than (3). No interconversion between the acylated compounds (11) and (12) could be observed, demonstrating that *N*-formyl- or *N*-thioformyl-sarcosine-*N*-methylthioamide (1; Y = O or S) are acylated at the thioamide nitrogen prior to their cyclization. The subsequent steps are outlined in Scheme 3.



SCHEME 3

The trifluoroacetylthioimidazolium ion (12; R = CF_3CO) is instantaneously deacylated in contact with water, whereas the corresponding acetyl compound is completely hydrolysed after some hours at room temperature. The trifluoroacetylaminothiazolium ion (11; R = CF_3CO) deacylates within hours, while the corresponding acetyl compound is stable in aqueous solution. The faster hydrolysis of acylthioimidazolium ions agrees with the fact that the mercaptoimidazolium ion (5) is more acidic than the aminothiazolium ion (3). This also explains why (5) is more readily acylated than (3), acylation involving deprotonation. The ready hydrolysis of the trifluoroacetylaminothiazolium ion (11; R = MeCO) offers a convenient procedure for the preparation of the pure aminothiazolium ion (3). The acetyl group of the acetylaminothiazolium ion (11; R = MeCO) reduces the basicity of the 4-position, and no exchange of H-4 takes place, even in deuteriotrifluoroacetic acid. H-2 of (11; R = MeCO) is exchanged in neutral D_2O as is H-2 of the aminothiazolium ion (3). The acetylaminothiazolium ion decomposes in aqueous base.

The observed behaviour of the aminothiazolium ion (3) allows rationalization of the previously reported transformations of 5-methylthiothiazolium ions (16) which on treatment with primary aliphatic amines give rise to *anhydro*-mercaptoimidazolium hydroxides (18), while aniline converts (16) to methylthioimidazolium salts (17).[3,4] These processes also are probably initiated by addition to C-2 of the thiazolium nucleus (Scheme 4). Subsequent ring-cleavage and recrystallization produce (15). Weak bases, like aniline, allow protonation of the sulphur atom which is followed by elimination of hydrogen sulphide. Stronger bases do not permit protonation of sulphur. Hence, elimination of methanethiol with formation of *anhydro*-mercaptoimidazolium hydroxides (18) occurs. In the latter case, an alternative initial substitution of the methylthio-group with amine to give an aminothiazolium ion like (3), which, in turn, *via* attack at C-2, rearranges to (18), is a very unlikely process, inasmuch as secondary amines do not replace methylthio-groups in methylthiothiazolium salts.[4] Secondary amines leave methylthiothiazolium salts unchanged. This appears reasonable, since possible C-2 adducts are unable to lose a proton in the ring-cleavage step. Nor is ring fission, as shown in Scheme 2, feasible in 2-substituted methylthiothiazolium salts (16). The fact that aromatic amines do not react with annellated methylthiazolium salts[4] may be explained by insufficient nucleophilic strength, or steric hindrance of attack at C-2 of the thiazole ring.

The present results account for the condensation of *NN'*-disubstituted glycinethioamides to *anhydro*-mercaptoimidazolium hydroxides.[5] The glycinethioamides are undoubtedly acylated to intermediates analogous to (1), followed by cyclization of the latter.

EXPERIMENTAL

Solvents were removed *in vacuo*. Purity and identity of all compounds were established through m.p. data, and i.r. and ^1H n.m.r. spectra. Hydrogen-1 and ^{13}C n.m.r. spectra were recorded on Bruker HX-90 and WH-90 instruments.

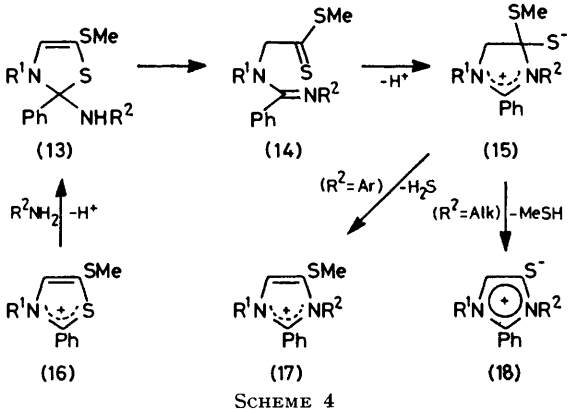
TABLE 2

Carbon-13 n.m.r. chemical shifts (p.p.m. relative to the dioxan peak at δ 67.4) and in parentheses one-bond ^{13}C–^1H coupling constants (Hz) of mercaptoimidazolium and amino-derivatives in aqueous solution [a]

Compound	C-2	C-4	C-5	*endo*-NMe	*exo*-NMe
(5) [b]	140.2 (226)	126.1	129.9 (202)	37.2 34.8	
(6)	134.5 (214)	141.2	120.7 (201)	36.2 33.6	
(3) [b]	141.5 (213)	113.1 (202)	156.1	43.0	33.9

[a] Signals were assigned through the coupled spectra; the quaternary carbon-atom signal as that showing no $^1J_{CH}$, and the C-2 signal as that having the largest value of $^1J_{CH}$. [b] As the trifluoroacetate.

N.m.r. data for mercaptoimidazolium and aminothiazolium derivatives are given in Tables 1 and 2. Low- and high-resolution mass spectra were obtained on Perkin-Elmer 270 and A.E.I. MS 3074 instruments respectively.



SCHEME 4

Starting Materials.—Sarcosine-*N*-methylthioamide hydrochloride (see below) (474 mg), recrystallized potassium dithioformate [8] (398 mg), chloroform (50 ml), and water (5 ml) were stirred together for 10 min. The organic phase was isolated and the aqueous solution extracted with chloroform (2 × 20 ml). The solvent was removed, the residue dissolved in ethyl acetate (20 ml), and the solution filtered through silica gel (10 g, Merck 0.05—0.2 mm). The silica gel was extracted with ethyl acetate (4 × 10 ml), the extract filtered through activated carbon, the solvent removed, and the residue recrystallized (ethyl acetate–hexane) to give 365 mg (74%) of N-*thioformylsarcosine*-N-*methylthioamide* (1; Y = S), colourless crystals, m.p. 96—98 °C (Found: C, 36.80; H, 6.20; N, 17.30; S, 39.00. $C_5H_{10}N_2S_2$ requires C, 37.05; H, 6.20; N, 17.30; S, 39.50%); *m/e* 162 (23%, M^+), 129 (100), 89, 88, 56, 44, and 42; $\delta_H(CDCl_3)$, conformer A: 9.27 (1 H, s, CHS), *ca.* 8.89 (1 H, br s, exchangeable, NH), 4.94 (2 H, s, CH_2), 3.47 (3 H, s, thioformamide-Me), and 3.13 (3 H, d, *J* 4.8 Hz, collapses on irradiation at 8.89, thioamide-Me); conformer B: 9.39, *ca.* 8.89, 4.63, 3.19, and 3.27 (d, *J* 4.7 Hz). Ratio of A : B is 6.2 : 1. With exception of the characteristic thioformyl absorption, these shifts are similar to those of *N*-formylsarcosine-*N*-methylthioamide (1), also existing in solution as a mixture of two rotamers.[6]

Preparative Transformations in Acid.—(*a*) *N*-Formylsarcosine-*N*-methylthioamide (1; Y = O) [6] (208 mg) was heated to reflux in 70% aqueous trifluoroacetic acid (2.8 ml) for 1 h. The solvent was removed, the residue dried at 0.13 kPa over potassium hydroxide for 1 d, and then over phosphorus pentaoxide for 1 d. Recrystallization [dichloromethane (2 ml)–ether (20 ml) with cooling to −25 °C for 1 h] gave 345 mg (100%) of 1,3-*dimethyl*-4-*mercaptoimidazolium trifluoroacetate* (5), yellow crystals, m.p. 99—101 °C (Found: C, 34.55; H, 3.60; N, 11.40; S, 13.20; F, 23.45. $C_7H_9F_3N_2O_2S$ requires C, 34.70; H, 3.75; N, 11.55; S, 13.25; F, 23.55%); *m/e* 128.043 (2%, $[M - CF_3COOH]^+$ requires 128.041), 127, 114.028 $[M - CF_3COOMe]^+$ requires 114.025 2), 113.995 0 ($[CF_3COOH]^+$), 86, 44, and 42.

(*b*) *N*-Formylsarcosine-*N*-methylthioamide (1; Y = O) (234 mg), acetonitrile (2.3 ml), and trifluoroacetic acid (0.23 ml) were refluxed together for 3 h. Work-up as in (*a*) gave 301 mg (78%) of (5).

(*c*) *N*-Thioformylsarcosine-*N*-methylthioamide (1; Y = S) (140 mg), acetonitrile (dried over molecular sieve, 3 Å) (5 ml), and trifluoroacetic acid (0.20 ml) were heated to reflux for 1 h. Work-up as in (*a*) gave 127 mg (61%) of 3-*methyl*-5-*methylaminothiazolium trifluoroacetate* (3), colourless deliquescent crystals, m.p. 94—96 °C (Found: C, 34.65; H, 3.80; N, 11.70; S, 13.45; F, 23.50. $C_7H_9F_3N_2O_2S$ requires C, 34.70; H, 3.75; N, 11.55; S, 13.25; F, 23.55%); *m/e* 128.043 ($[M - CF_3COOH]^+$ requires 128.040 8), 118, 114.026 7 ($[M - CF_3COOMe]^+$ requires 114.025 2), 97, 95, 86, 69, 51, 50, 45, 44, and 42.

(*d*) Compound (1; Y = O) (38 mg) in hydrochloric acid (1%, 0.4 ml) was set aside for 28 d, and 1N sodium hydroxide (2 ml) was then added. Work-up as in (*e*) gave 69% of (8) (see below).

(*e*) Subjection of (3) to the conditions in (*a*), evaporation twice with hydrochloric acid (35%) to remove trifluoroacetic acid, and work-up as in (*a*) (below) gave 68% of (8).

Spectroscopic Experiments in Acid.—*N*-Formylsarcosine-*N*-methylthioamide (1) (40 mg) was dissolved in trifluoroacetic acid (0.40 ml). ^1H N.m.r. spectra indicated conversion of (1) into (3) and (5); no other products were detectable. Conversion was complete in 2 h. The ratio of (3) : (5) (1 : 1) remained constant during the reaction. *N*-Thioformylsarcosine-*N*-methylthioamide (1; Y = S) produced (3) and (7) (1 : 1.4) instantaneously under similar conditions. In either case, no significant change was observed after heating to 100 °C for 1 h. Addition of water (0.03 ml) and heating to 100 °C for 10 min gave (5) as the sole product. Pure (3), when heated in 70% aqueous trifluoroacetic acid to 100 °C for 10 min likewise gave (5), exclusively. All products were identified by addition of the pure substances to the solution

Reactions with Acetyl Chloride and Trifluoroacetic Anhydride.—(*a*) Finely ground (1) (54 mg) and acetyl chloride (1.0 ml) were stirred for 2 h. Removal of the acetyl chloride and washing with ethyl acetate (2 × 2 ml) gave 75 mg (100%) of 3-*methyl*-5-*methylacetylaminothiazolium chloride* (11; R = MeCO), colourless hygroscopic crystals, m.p. 196—197 °C. Recrystallization from methanol–ether did not raise the m.p. (Found: C, 40.15; H, 5.25; N, 13.30; S, 14.85. $C_7H_{11}ClN_2OS$ requires C, 40.65; H, 5.35; N, 13.55; S, 15.50%).

(*b*) *N*-Thioformylsarcosine-*N*-methylthioamide (1; Y = S) and acetyl chloride similarly gave (100%) of (11).

(*c*) *N*-Formylsarcosine-*N*-methylthioamide (1) (211 mg) and trifluoroacetic anhydride (1.0 ml) were mixed with cooling and set aside at 20 °C for 1 h. Removal of the solvent furnished 3-*methyl*-5-*trifluoroacetylmethylaminothiazolium trifluoroacetate* (11; R = CF_3CO) as a brown oil, not further purified (n.m.r. data in Table 1). Stirring with water (2.0 ml) for 3 h, removal of the water, and work-up as above yielded 304 mg (87%) of (3).

(*d*) 1,3-Dimethyl-4-mercaptoimidazolium trifluoroacetate (5) (100 mg) and acetyl chloride (1 ml) were stirred for 2 h. Removal of the acetyl chloride, washing with ether (2 × 10 ml), and drying (phosphorus pentaoxide, 0.13 kPa) afforded 136 mg of 4-*acetylthio*-1,3-*dimethylimidazolium chloride* and *trifluoroacetate* (12; R = MeCO), identified through its ^1H n.m.r. spectrum (Table 1). The compound hydrolysed in aqueous solution to (5) in 4 d at 20 °C.

(*e*) Analogously, (5) and trifluoroacetic anhydride produced 100% of 1,3-*dimethyl*-4-*trifluoroacetylthioimidazolium trifluoroacetate* (12; R = CF_3CO) as a dark oil (n.m.r. data in Table 1). The compound hydrolysed instantaneously in aqueous solution to (5).

(*f*) 3-Methyl-5-methylaminothiazolium trifluoroacetate (3) (85 mg) and acetyl chloride (1 ml) were set aside for 2 h. Work-up as in (*a*), followed by two evaporations with hydrochloric acid (35%, 1 ml) gave 72 mg (100%) of (11).

(*g*) Compound (3) and trifluoroacetic anhydride were set aside for 3 d and the mixture worked up as in (*b*) producing (11; R = CF_3CO) in quantitative yield.

Preparative Transformations in Base.—(*a*) *N*-Formylsarcosine-*N*-methylthioamide (1) (138 mg) in 1N sodium hydroxide (9 ml) was set aside for 3 h. The solvent was removed at room temperature and the residue extracted with ethyl acetate (3 × 5 ml). Filtration through activated carbon and removal of the solvent gave 85 mg (88%) of *sarcosine*-N-*methylthioamide* (8), sublimable at 96 °C (27 Pa); *m/e* 118 (53%, M^+), 89, 69, 45, and 44 (100%); $\delta_H(CDCl_3)$ 9.45 (1 H, br s, exchangeable, NH), 3.71 (2 H, s, CH_2), 3.25 (3 H, d, *J* 4.2 Hz, collapses on irradiation at 9.45, thioamide-Me), and 2.42 (3 H, s, NMe). The *hydrochloride* had m.p. 165—166 °C (acetonitrile) (Found: C,

13.20; H, 7.10; Cl, 22.85; S, 20.50; N, 18.10. $C_4H_{11}ClN_2S$ requires C, 31.05; H, 7.15; Cl, 22.90; S, 20.75; N, 18.10%).

(*b*) *N*-Thioformylsarcosine-*N*-methylthioamide (1; Y = S) (156 mg), methanol (10 ml), and a methanolic suspension of a strong basic ion-exchanger (Amberlite IRA 400, in the OH^--form) (10 ml) were stirred for 2 h. Filtration and removal of the solvent furnished 107 mg (87%) of anhydro-1,3-*dimethyl*-4-*mercaptoimidazolium hydroxide* (6), colourless crystals, m.p. 145—147 °C (decomp.). The material was dissolved in acetonitrile, filtered through activated carbon, and recrystallized (acetonitrile–ethyl acetate) to give m.p. 149—151 °C (decomp.) (Found: C, 45.50; H, 6.50; N, 21.55; S, 24.20. $C_5H_8N_2S$ requires C, 46.50; H, 6.30; N, 21.85; S, 25.00%); *m/e* 128.042 (100%) (M^+ requires 128.041), 86 (38%), and 42 (78); n.m.r. data in Tables.

(*c*) 2N Sodium hydroxide (3 ml) was added to an aqueous solution of (3) (94 mg in 1.5 ml). Removal of the solvent at 20 °C, extraction with acetonitrile (3 × 3 ml), removal of the acetonitrile, and washing with ether (3 × 4 ml) gave a residue (29 mg) of impure (6) (^{1}H n.m.r.). The ether solution contained 30 mg (75%) of (8).

(*d*) 1,3-Dimethyl-4-mercaptoimidazolium trifluoroacetate (5) (100 mg) and 6,6-dimethylpyridine, containing 7% of 4-methylpyridine (1.5 ml), were heated to 70 °C for 5 min. Removal of the solvent, drying (phosphorus pentaoxide, 0.13 kPa), washing with benzene (3 × 2 ml), and then ethyl acetate (3 × 1 ml) left 35 mg (45%) of anhydro-1,3-*dimethyl*-5-(1,3-*dimethylimidazolium*-4-*thio*)-4-*mercaptoimidazolium hydroxide trifluoroacetate* (7), m.p. 136—146 °C. Recrystallization (acetonitrile–ethyl acetate) gave colourless crystals, m.p. 158 °C (Found: C, 38.95; H, 4.00; N, 15.25; S, 17.35; F, 15.65. $C_{12}H_{15}N_4F_3O_2S_2$ requires C, 39.10; H, 4.10; N, 15.20; S, 17.40; F, 17.45%); *m/e* 254.064 (27%) ($[M - CF_3COOH]^+$ requires 254.066); $\delta_H(D_2O)$ 8.84 (1 H, d, *J* 1.3 Hz, rapidly exchangeable at pD 7, H-2), 8.62 (1 H, s, slowly exchangeable at pD 14, H-2′), 7.85 (1 H, d, *J* 1.3 Hz, slowly exchangeable at pD 7, H-5), 4.03, 3.89, 3.84, and 3.68 (12 H, s, 4 NMe); $\delta_C(H_2O)$ 151.9 (s, C-4′), 139.3 (d, $^1J_{CH}$ 213 Hz, C-2′), 136.7 (d, $^1J_{CH}$ 222 Hz, C-2), 128.6 (d, $^1J_{CH}$ 201 Hz, C-5), 126.2 (s, C-4), 116.3 (s, C-5′), and 37.0, 35.6, 34.9, and 34.6 (4 q, 4 NMe).

Spectroscopic Experiments in Base.—(*a*) *N*-Thioformylsarcosine-*N*-methylthioamide (1; Y = S) (20 mg) was dissolved in a 1N solution of sodium hydroxide in D_2O (0.5 ml). ^{1}H N.m.r. spectra indicated that *anhydro*-1,3-dimethyl-4-mercaptoimidazolium hydroxide (6) was formed instantaneously as the sole product.

(*b*) 1,3-Dimethyl-4-mercaptoimidazolium trifluoroacetate (5) (20 mg) was dissolved in D_2O (0.1 ml) and a 2N-solution of sodium hydroxide in D_2O (0.5 ml) was added. ^{1}H N.m.r. spectra revealed that all the (5) had been transformed into (6). No other products could be detected.

(*c*) *N*-Formylsarcosine-*N*-methylthioamide (1) (20 mg), CD_3CN (0.40 ml), and triethylamine (0.040 ml), both dried over a molecular sieve (3 Å), were heated to 110 °C for 3 h. ^{1}H N.m.r. spectra revealed that (1) was unchanged.

(*d*) *N*-Thioformylsarcosine-*N*-methylthioamide (1; Y = S) (20 mg), in dry CD_3CN–triethylamine (10 : 1) (0.44 ml), was converted quantitatively into (6) in 6 h at 20 °C.

(*e*) 3-Methyl-5-methylaminothiazolium trifluoroacetate (3) (22 mg) and sodium hydrogencarbonate (10 mg) in water (0.40 ml) (pH 7) were set aside at 20 °C. ^{1}H N.m.r. spectra indicated conversion to the adduct (2) (Table 1). The reaction ceased after 3 d at a ratio of (2) : (3) of 1 : 1. Addition of more base did not increase the ratio but led to formation of (8). Addition of acid led to reconversion of (2) into (3).

(*f*) 3-Methyl-5-methylaminothiazolium trifluoroacetate (3) (63 mg) was set aside in CD_3CN (0.40 ml) containing propylamine (0.040 ml), both dried over molecular sieves (3 Å). ^{1}H N.m.r. indicated rapid formation of (6). After *ca.* 10 min, signals from (7) emerged. Complete conversion of (3) into a 2.4 : 1 mixture of (6) and (7) was achieved in *ca.* 12 h. All products, with the exception of (2), were identified by addition of the pure substances to the solution.

I thank Dr. J. Øgaard Madsen for the mass spectra, Dr. L. Dalgård for high-resolution mass spectra, Dr. S. Refn for the i.r. spectra, and Professor A. Kjær for help with the manuscript.

[8/388 *Received*, 2*nd March*, 1978]

REFERENCES

[1] R. Huisgen, E. Funke, F. C. Schaeffer, H. Gotthardt, and E. Brunn, *Tetrahedron Letters*, 1967, 1809.
[2] K. T. Potts and D. N. Roy, *Chem. Comm.*, 1968, 1062.
[3] T. Shiba and H. Kato, *Bull. Chem. Soc. Japan*, 1970, **43**, 3941.
[4] P. B. Talukdar, S. K. Sengupta, and A. K. Datta, *Indian J. Chem.*, 1973, **11**, 1257.
[5] R. Grashey, E. Jänchen, and J. Litzke, *Chem.-Ztg.*, 1973, **97**, 657.
[6] M. Begtrup, *J.C.S. Perkin I*, 1979, 521.
[7] R. A. Olofson, W. R. Thompson, and J. S. Michelman, *J. Amer. Chem. Soc.*, 1964, **86**, 1865.
[8] T. G. Levi, *Gazzetta*, 1924, **54**, 395.