Reactions of *S*-Alkyl-*N,N*-disubstituted Thioamide Salts. Part 4.[1] Sulphenamidine Derivatives

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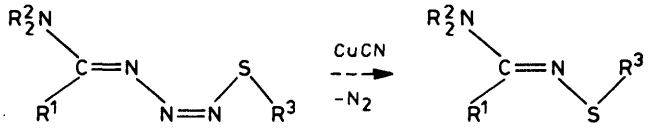
Readily available 3-(α-dialkylaminoalkylidene)-1-alkylthiotriazenes (**1**) with C-aryl, benzyl, or isopropyl substituents, on being stirred with copper(I) cyanide or copper powder in dichloromethane or toluene solution at room temperature or below, give sulphenamidines (**2**) whose properties have been investigated. A mechanism for this extrusion reaction is suggested.

Thioamides are obtainable by several methods,[2,3] perhaps the simplest being the Willgerodt–Kindler reaction, whose versatility has been further extended by the use of volatile amines as their hydrochlorides with sodium acetate in dimethylformamide (DMF) solution, thus obviating the need, with them, for the use of closed vessels.[3] The *N,N*-dialkylthioamides react with iodoalkanes, under mild conditions, to give good yields of stable, crystalline *S*-alkyl salts, which are useful intermediates since they react with a wide variety of nucleophiles.[2] In particular, with nitrogen nucleophiles, they can be used for the preparation of various amidine derivatives.[2a,4,5] With sodium azide in aqueous solution at room temperature they give crystalline compounds, originally formulated as thia(S^{IV})triazoles,[6,†] but later shown by *X*-ray crystal analysis[7] to be 3-(α-dialkylaminoalkylidene)-1-alkylthiotriazenes (**1**).



(**1a–j**) (**2a–h**)

	R^1	NR_2^2	R^3
(**1**) + (**2**)	**a**; Ph	morph[a]	Me
	b; Ph	NMe_2	Me
	c; Ph	morph	CH_2Ph
	d; 4-$MeOC_6H_4$	NMe_2	Me
	e; 4-ClC_6H_4	NMe_2	Et
	f; See Scheme 1		
	g; $PhCH_2$	morph	Me
	h; Pr^i	morph	Me
(**1j**)	Me	NMe_2	Et

[a] Morpholino.

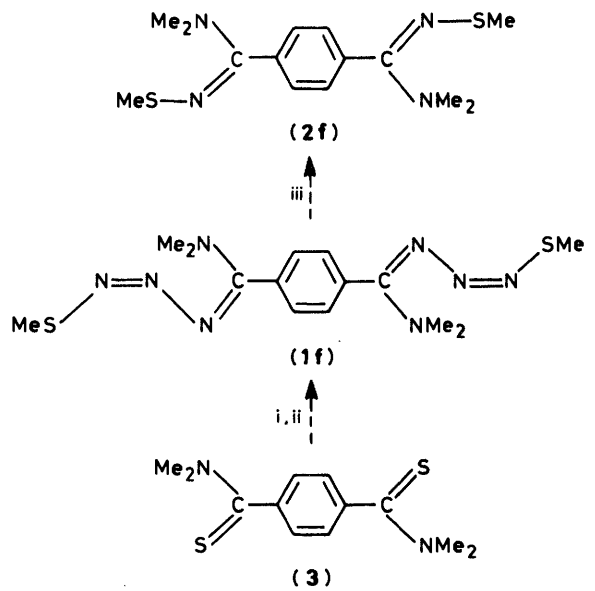
As we briefly reported,[8] these readily evolve nitrogen in dichloromethane solution at room temperature or below, in the presence of copper(I) cyanide as catalyst, giving good yields of the corresponding sulphenamidine (**2**). Compound (**2b**) was shown by *X*-ray analysis to be (*E*)-N^1,N^1-dimethyl-N^2-methylthiobenzamidine.[8] This reaction in dichloromethane is generally applicable when a *C*-aryl group is present (Table 1) including the case of the bistriazene from the terephthalamide derivative (**3**) (Scheme 1), but with benzyl- or alkyl-triazenes, although nitrogen is evolved, formation of dark copper complexes occurs, and no sulphenamidine was isolated. The product from triazene (**1j**) gave diethyl disulphide in fair yield, presumably from a radical reaction. However, when toluene was substituted for dichloromethane as solvent, the catalytic extrusion occurred normally, but more slowly, with phenethyl-

† IUPAC recommendation: 5*H*-1λ⁴,2,3,4-thiatriazoles.

Table 1. Sulphenamidines (**2**)

	Yield %	M.p. (°C)	Elemental analysis[a] (%) C	H	N
(**2a**)	84[b]	84	61.1 (61.0)	6.9 (6.8)	11.9 (11.85)
(**2b**)	75[b]	95—96	61.9 (61.85)	7.4 (7.2)	14.4 (14.4)
(**2c**)	38[b]	90—91	69.1 (69.2)	6.6 (6.4)	8.9 (8.95)
(**2d**)	47[c]	64	59.1 (58.9)	2.25 (7.15)	12.25 (12.5)
(**2e**)	87[b]	49—50	54.5 (54.4)	6.2 (6.2)	11.4 (11.55)
(**2f**)	45[b]	154	54.3 (54.2)	7.0 (7.1)	17.85 (18.05)
(**2g**)	75[b]	65—66	62.3 (62.4)	7.2 (7.2)	11.1 (11.2)
(**2h**)	92[d]	43—45	53.45 (53.5)	9.3 (8.9)	13.7 (13.85)

[a] Required values in parentheses. [b] Yield based on triazene. [c] Yield based on quaternary salt. [d] Yield of crude product.

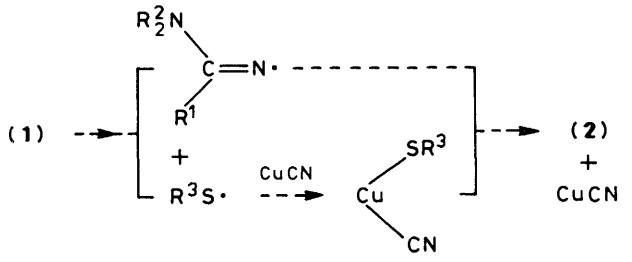


Scheme 1. *Reagents:* i, MeI; ii, aq. NaN_3; iii, CuCN in CH_2Cl_2

idene- and isobutylidene-triazenes (**1g** and **h**) giving, cleanly, the corresponding sulphenamidines in good yield. Copper powder may replace the copper(I) cyanide, but the reaction is slower.

Table 2. Spectral properties of sulphenamidines (**2**)

	Mass (*m/z*) (b = base)	U.v. ($\lambda_{max.}$/nm) (hexane)	I.r. ($\nu_{max.}$ cm^{-1}) (Nujol)	^1H N.m.r. ($CDCl_3$) δ (*J*/Hz)
(**2a**)	236 (M^+) 86 (b, morph)	310 ε 2 900	1 560s, 1.260s, 1 110s	7.4 (5 H, m, ArH), 3.65 (4 H, m, 2 CH_2O), 3.25 (4 H, m, 2 CH_2N), 2.53 (3 H, s, SMe)
(**2b**)	194 (M^+) 44 (b, NMe_2)	314 ε 2 200	1 560s, 1 099m, 770s	7.5 (3 H, m, ArH *m*- and *p*-), 7.3 (2 H, m, ArH *o*-), 2.84 (6 H, s, NMe_2), 2.56 (3 H, s, SMe)
(**2c**)	312 (M^+) 86 (b, morph)	308 ε 3 400	1 560s, 1 260s, 1 120s	7.3 (10 H, m, ArH), 4.05 (2 H, s, SCH_2), 3.6 (4 H, m, 2 CH_2O), 3.2 (4 H, m, 2 CH_2N)
(**2d**)	224 (M^+, also b)	294 (sh) ε 3 600	1 570s, 1 250s, 1 080m	7.18 (2 H, d, *J* 9, ArH *o*- to C=N), 6.90 (2 H, d, *J* 9, ArH *o*- to OMe), 3.73 (3 H, s, OMe), 2.76 (6 H, s, NMe_2), 2.48 (3 H, s, SMe)
(**2e**)	242, 244 (M^+) 44 (b, NMe_2)	324 ε 2 100	1 560s, 1 080s, 850s	7.35 (2 H, d, *J* 9, ArH *o*- to Cl), 7.13 (2 H, d, *J* 9, ArH *o*- to C=N), 2.85 (2 H, q, CH_2), 2.75 (6 H, s, NMe_2), 1.27 (3 H, t, CMe)
(**2f**)	310 (M^+) 44 (b, NMe_2)	326 ε 3 400	1 560s, 1 090m, 930m	7.29 (4 H, s, ArH), 2.83 (12 H, s, 2 NMe_2), 2.55 (6 H, s, 2 SMe)
(**2g**)	250 (M^+) 86 (b, morph)	265 ε 7 500	1 585s, 1 120s, 970s	7.24 (5 H, s, ArH), 3.93 (2 H, s, $ArCH_2$), 3.6 (4 H, m, 2 CH_2O), 3.3 (4 H, m, 2 CH_2N), 2.60 (3 H, s, SMe)
(**2h**)	202 (M^+) 86 (b, morph)	265 ε 6 100	1 580s, 1 120s, 1 030m	3.65 (4 H, m, 2 CH_2O), 3.15 (4 H, m, 2 CH_2N), 2.56 (3 H, s, SMe), 2.5 (1 H, m, CH), 1.22 (6 H, d, *J* 7, CMe_2)



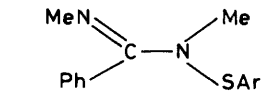
Scheme 2.

The mechanism may involve fission of the triazenes (**1**) giving nitrogen together with two radicals (Scheme 2). The *S*-alkyl radical could be stabilised as the mixed copper(II) derivative, which, with the amidine radical, might then give the sulphenamidine, re-forming the copper(I) cyanide. Attempted crossover experiments to test this have been unsuccessful, since the sulphenamidines decomposed on t.l.c. plates, and mixtures of them equilibrate thermally, as shown below. A somewhat similar oxidation–reduction mechanism has been postulated for the Sandmeyer reaction.[9]

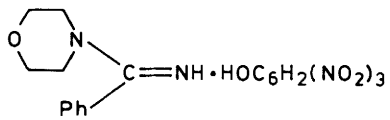
Sulphenamidines of structure (**2**) appear to be unknown, but the double-bond isomers (**4**) with *S*-aryl substituents have been prepared[10] by reaction of N^1,N^2-dimethylbenzamidine with arenesulphenyl chlorides.

The sulphenamidines (**2**) give large, almost colourless crystals from light petroleum. Compound (**2a**) was heated at 170 °C for 1 h in an open tube, and, on cooling, the melt re-solidified with unchanged ^1H n.m.r. spectrum. However, the N–S bond is thermally labile, as shown by g.c. experiments with a capillary column, using an inert stationary phase and programmed from 100—260 °C. The sulphenamidine (**2b**) gave a single sharp peak, and, as expected, a mixture of compounds (**2b** and **d**), both of which have N–SMe groups, gave two peaks. However, under the same conditions, a mixture of compounds (**2b** and **e**), which differ from each other on both sides of the N–S bond, gave four sharp peaks, showing that fission at this bond, with equilibration, had occurred.

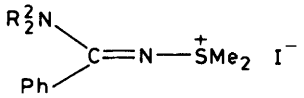
The N–S bond is also readily cleaved by acid, as shown by the rapid and quantitative formation, at room temperature, of the amidine picrate (**5**) by treatment of the sulphenamidine (**2a**) with ethanolic picric acid. The same picrate is formed likewise, with nitrogen evolution, by the parent triazene.[6]



(**4**)



(**5**)



(**6**)

The sulphenamidines (**2a** and **b**) reacted readily with excess of iodomethane at room temperature, giving the sulphonium salts (**6a** and **b**), whose ^1H n.m.r. spectra show six-proton singlets (SMe_2) at δ 3.08 and 3.12, respectively, showing that methylation had occurred on sulphur.

The spectral data of the sulphenamidines are shown in Table 2. All give strong i.r. absorption as Nujol mulls in the range 1 560—1 580 cm^{-1}, and moderately intense u.v. absorption in hexane, usually at just over 300 nm in the case of *C*-aryl compounds, but at 265 nm for the *C*-benzyl and -isopropyl analogues. The mass spectra show prominent molecular ion peaks, but the dialkylamino groups usually form the base peaks.

Experimental

U.v. and i.r. spectra were recorded on Perkin-Elmer 402 and Pye-Unicam SP3-200 instruments, respectively. ^1H N.m.r. spectra at 60 MHz were obtained in $CDCl_3$ with a Perkin-Elmer

R 12B instrument, and mass spectra with an A.E.I. MS 30 spectrometer, using a direct-insertion probe at 70 e.V.

G.c. experiments were carried out using a 25 m capillary column with wall-coated fused-silica crossbonded OV-1 stationary phase, in hydrogen gas, and programmed from 100—260 °C at 5 °C min^{-1}.

Thioamides.—*N,N*-Dimethylthioacetamide was obtained by reaction of the amide with phosphorus pentasulphide in carbon disulphide solution.[2a] All the other thioamides were made from the aldehyde or ketone by the Willgerodt–Kindler reaction, those having a dimethylamino group by the Amupitan modification.[3]

Thus terephthalaldehyde (8.04 g, 60 mmol), dimethylammonium chloride (14.66 g, 180 mmol), anhydrous sodium acetate (14.76 g, 180 mmol), and sulphur (5.76 g, 180 mg-atom), in DMF (40 ml) were heated on a steam-bath, and occasionally swirled, for 3 h, water (100 ml) was added, and after being ice-cooled and shaken, the product was filtered off, washed with water, dried, and crystallised from glacial acetic acid (400 ml; charcoal) to give *N,N,N',N'*-tetramethyldithioterephthalamide (**3**) as fine yellow needles (12.95 g, 86%), m.p. 254 °C (lit.,[2c] 248—251 °C) (Found: C, 57.4; H, 6.5; N, 10.8. Calc. for $C_{12}H_{16}N_2S_2$: C, 57.15; H, 6.35; N, 11.1%); δ 7.28 (4 H, s, ArH), and 3.58 and 3.19 (each 6 H, s, 2 NMe).

Quaternary Salts.—These were made by reaction of the thioamides with the iodoalkane (3 equiv.) in boiling acetone,[2a] or, for the *S*-benzyl salt, by heating with neat benzyl bromide on a steam-bath.

Triazenes (**1**).—Aqueous solutions of the crude quaternary salts were filtered onto solid sodium azide (8 equiv.), and after being swirled to dissolve the latter, the mixtures were kept at room temperature for 5 h to afford crystalline triazenes,[6] which were filtered off, washed with water, and dried. They could be stored indefinitely in a refrigerator. Alternatively, without isolation, they could be extracted into dichloromethane or toluene, and the solutions washed, dried, and used directly.

Preparation of Sulphenamidines (**2**). *General Procedure.*—(*a*) An ice-cooled solution of the triazene (**1a**—**f**) (20 mmol) in dichloromethane (100 ml) was stirred and copper(I) cyanide (30 mmol) was added all at once. Vigorous nitrogen evolution occurred, and was complete after *ca.* 0.5 h. The mixture was stirred for a further 1 h and the copper salt was filtered off. The solvent was removed under reduced pressure from the yellow filtrate, and the residue, which often solidified, was crystallised from light petroleum (b.p. 60—80 °C; 30 ml), the solution being filtered whilst hot to remove a small amount of copper derivative.

The dark filtrate from reaction of the triazene (**1j**), after being shaken with aqueous 1,2-diaminoethane, was evaporated, and the residue was chromatographed in pentane on a Bentonite–Kieselguhr column to give diethyl disulphide, b.p. 156 °C (lit.,[11] 154 °C); δ 2.70 (4 H, q, 2 CH_2) and 1.30 (6 H, t, 2 CH_3).

(*b*) A similar procedure was used for triazenes (**1g** and **h**), but toluene (60 ml) was substituted for dichloromethane. The mixture was stirred, with evolution of N_2 for 20 h, and work-up was as above. The sulphenamidine (**1h**) did not crystallise, so the light petroleum solution was evaporated, and the remaining yellow oil was cooled and triturated with pentane (3 ml), and the crystals filtered off, washed with cold pentane, and dried.

Reaction of Sulphenamidine (**2a**) *with Picric Acid.*—Compound (**2a**) (0.50 g) was added to an excess of ethanolic picric acid, the mixture was kept at room temperature for 2 h, the product was filtered off, washed with cold ethanol, and dried to yield the picrate of α-morpholinobenzylideneamine (**5**) as yellow rhombs (0.85 g, 99%), m.p. 204 °C (lit.,[6] 203 °C), identical with the product from the parent triazene.[6]

Reaction of Sulphenamidines with Iodomethane.—Compound (**2a**) (0.30 g) was dissolved in iodomethane (5 ml). The initially clear yellow solution rapidly became turbid due to separation of the product. After 1 h the iodomethane was evaporated off and the colourless crystals were triturated with diethyl ether to give, quantitatively, the *sulphonium iodide* (**6a**), m.p. 154 °C (from acetone) (Found: C, 41.15; H, 5.05; N, 7.2. $C_{13}H_{19}IN_2OS$ requires C, 41.3; H, 5.0; N, 7.4%); δ 7.55 (5 H, s, ArH), 3.0—4.2 (8 H, m, morpholino), and 3.12 (6 H, s, SMe_2). It is very soluble in water.

Similarly the sulphenamidine (**2b**) gave, in 98% yield, the *sulphonium iodide* (**6a**), m.p. 117 °C. This, unlike compound (**6a**), is very soluble in acetone, and a sample was crystallised from a small volume of propan-2-ol and dried at 80 °C/0.1 mmHg (Found: C, 38.8; H, 5.1; N, 8.1. $C_{11}H_{17}IN_2S$ requires C, 39.3; H, 5.1; N, 8.3%); δ 7.5 (5 H, m, ArH), 3.20 and 2.94 (each 3 H, s, NMe), and 3.08 (6 H, s, SMe_2).

Acknowledgements

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References

1 Part 3, F. Stansfield and M. D. Coomassie, *J. Chem. Soc., Perkin Trans. 1*, 1979, 2708.
2 (*a*) Part 1, D. A. Peak and F. Stansfield, *J. Chem. Soc.*, 1952, 4067; (*b*) Part 2, S. A. Okecha and F. Stansfield, *J. Chem. Soc., Perkin Trans. 1*, 1977, 1811; (*c*) J. P. Brown and (Mrs) M. Thompson, *ibid.*, 1974, 863.
3 J. O. Amupitan, *Synthesis*, 1983, 730, and references therein.
4 S. A. Okecha, *Chem. Ind. (London)*, 1979, 526.
5 J. O. Amupitan and F. Stansfield, unpublished results.
6 (Mrs) S. I. Mathew and F. Stansfield, *J. Chem. Soc., Perkin Trans. 1*, 1974, 540.
7 R. L. Beddoes and O. S. Mills, *J. Chem. Res.*, 1981, (*S*) 132; (*M*) 1701.
8 R. L. Beddoes, R. J. Cernik, O. S. Mills, and F. Stansfield, *J. Chem. Soc., Chem. Commun.*, 1983, 390.
9 S. C. Dickerman, D. J. DeSouza, and N. Jacobson, *J. Org. Chem.*, 1969, **34**, 710.
10 K. Hartke and H.-M. Wolff, *Chem. Ber.*, 1980, **113**, 1394.
11 R. Nasini, *Ber. Dtsch. Chem. Ges.*, 1882, **15**, 2882.

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