1,2,4-Dithiazole-3-thiones and derivatives

J. W. MacDonald
Department of Chemistry, Dalhousie University, Halifax, Nova Scotia

AND

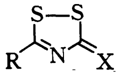
D. M. McKinnon
Department of Chemistry, University of Manitoba, Winnipeg, Manitoba

Received October 14, 1966

5-Aryl-1,2,4-dithiazole-3-thiones may be made by sulfurization of *N*-aroyl-isothiocyanates, -thionocarbamates, or -dithiocarbamates. Attempts to produce 5-alkyl compounds failed, whereas an alternate cyclization of a reaction intermediate produced a 1,3-thiazine from cinnamoyl isothiocyanate. The mechanisms of the reactions are discussed briefly. The thiones readily form adducts with methyl iodide and reactive acetylenes. In the latter case, 1,3-dithiole derivatives are obtained.

Canadian Journal of Chemistry. Volume **45**, 1225 (1967)

1,2,4-Dithiazoles have not been studied extensively, but some derivatives have been reported. The oxidation of dithiobiurets (1) or trithioallophthanic acid (2) with halogen produced 5-amino- and 5-alkylthio-3-imino-1,2,4-dithiazoles (I*a* and I*b*), respectively, and crystallographic studies (3) have confirmed that "isoperthiocyanic acid" exists as 5-amino-1,2,4-dithiazole-3-thione (I*c*). 2,5-Diamino-3,4-diazathiothiophthene (I*d*) (4) may also be regarded as a 1,2,4-dithiazole derivative.



I*a* R = NH_2, X = NH
I*b* R = S·alkyl, X = NH
I*c* R = NH_2, X = S
I*d* R = NH·alkyl, X = NCSNH·alkyl

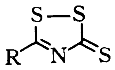
However, no derivatives of the system containing a carbon atom directly attached to the heterocyclic ring had been reported until recently, when the 1,2,4-dithiazole-3-thione system was made by the sulfurization in xylene of *N*-acylthioureas, *N*-acylisothiocyanates, *N*-acyldithiocarbamates, and 2-aryl-1,3-thiazoline-4,5-diones (5).

Independently, we have confirmed the above reactions by similar syntheses, and have prepared some other derivatives. Some reactions of the system have also been investigated.

Three methods of preparation of such 1,2,4-dithiazole-3-thiones (III) were successful. Treatment of aroyl isothiocyanates (II), prepared from lead thiocyanates and the appropriate acid chloride (6), with excess phosphorus pentasulfide in boiling carbon disulfide gave the thiones in a rather low yield, accompanied by varying amounts of by-products, mostly nitriles; the reaction times varied from 20 to 120 min. Usually the reactions were stopped when the color of the reaction mixture became a deep reddish brown. The use of a higher boiling medium, e.g. toluene, increased the reaction rate, but the amounts of tarry by-products were also raised.

RCONCS →

II



III

a R = C_6H_5
b R = C_6H_4·*p*-CH_3
c R = C_6H_4·*o*-CH_3
d R = C_6H_3·2,5-$(CH_3)_2$
e R = C_6H_4·*p*-OCH_3
f R = C_6H_4·*o*-Cl
g R = C_6H_4·*p*-Cl
h R = 2-furyl
i R = 2-thienyl
j R = 1-naphthyl
k R = 2-naphthyl

Better yields were obtained by the sulfurization in benzene of *S*-methyl *N*-aroyldithiocarbamates (IV*b*), prepared (7) by the reaction of methanethiol with the appropriate aroyl isothiocyanate. Thiones were also obtained, but in a very low yield, by the sulfurization of *O*-methyl *N*-aroylthionocarbamates (IV*a*) in benzene. The main products were thiobenzamide, methyl benzoate, and sulfur. This method held no advantage over the first two. An attempted preparation of thione from benzoylthiourea failed.

The scope of the first two methods is fairly wide. Various substituted phenyl derivatives (III*a*–III*g*) were prepared. Also, two products bearing hetero rings (III*h* and III*i*) were prepared. However, the preparations failed where the acyl group was aliphatic (i.e. II, R = benzyl, diphenylmethyl, ethyl, and *t*-butyl), indicating that a stabilizing aromatic group or its equivalent was necessary.

Sulfurization of cinnamoyl isothiocyanate (II, R = styryl) gave no 1,2,4-dithiazole-3-thione. Instead, 6-phenyl-4-hydroxy-5,6-dihydro-1,3-thiazine-2-thione (V), or possibly a tautomer, was obtained. Its structure was assigned on the basis of its analysis and proton magnetic resonance spectrum. This showed a band at 2.66 τ assigned to the protons of the phenyl ring. A triplet centered at 5.30 τ was assigned to the proton on carbon 6, and a singlet at 6.73 τ and a closely spaced doublet (splitting 5 c.p.s.) at 6.83 τ were assigned to the protons of the methylene group. One of them was split by the single proton on the adjacent carbon atom. A broad peak at 0.43 τ was assigned to the proton of the hydroxy group.

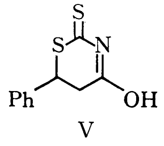
This compound was probably formed by cyclization of an initially formed cinnamoyldithiocarbamic acid, involving internal β-addition of the —SH of the dithio acid. Such β-addition of thiols to α,β-unsaturated carbonyl compounds is well known (8), and in a related reaction (9) ammonium dithiocarbamate reacts readily with an α,β-unsaturated compound such as mesityl oxide to produce another 1,3-thiazine derivative. Sulfurization of methyl cinnamoyldithiocarbamate according to the second procedure gave only tars.

Attempts to produce 5-phenyl-1,2,4-dithiazole-3-thione by sulfurization of thiobenzoyl isocyanate (10) were unsuccessful, whereas the attempted generation of isocyanate *in situ* by the direct sulfurization of 2-phenyl-1,3-thiazoline-4,5-dione in benzene gave a product whose analysis did not correspond to any simple product. This was in marked contrast to the results of Derocque and Viaille (5), who obtained 5-aryl-1,2,4-dithiazole-3-thiones in varying yields by this method. The products of the reaction are probably temperature dependent.

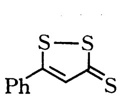
The thiones range in color from orange to dark red. They are stable for several months, and may be recrystallized from most common solvents, but they decompose at elevated temperatures to sulfur, carbon disulfide, and the corresponding nitrile. Their odors are reminiscent of the related 1,2-dithiole-3-thiones (VI), of which they are 4-aza analogues.

ArCONHCSR

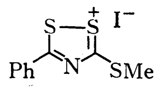
IV*a* R = OCH_3
IV*b* R = SCH_3
IV*c* R = NH_2



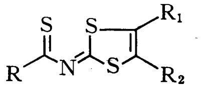
V



VI



VII



VIII*a* R = Ph, $R_1 = CO_2Et$, R_2 = H
VIII*b* R = Ph, $R_1 = CO_2Et$, R_2 = Ph
VIII*c* R = Ph, $R_1 = R_2 = CO_2Me$
VIII*d* R = Ph, R_1,R_2 = —$[CH{=}CH]_2$—
VIII*e* R = 2-thienyl, $R_1 = CO_2Et$, R_2 = H

That the aromatic ring was intact and cyclization had not occurred in an alternative way was demonstrated by the reaction of the 5-phenyl compound III*a* with ammonia or aniline. The resulting products were thiobenzamide and *N*-phenylthiobenzamide, respectively. These presumably arose by nucleophilic attack of the amines at position 5 of the heterocyclic ring, followed by ring fission. Elemental sulfur was also detected in the reaction products. The fate of the other fragment of the molecule is not known, but thiocyanate ion was not detectable in the products.

The structure of the thione III*a* was also indicated by mass spectral data (mol. wt. 211), and by the proton magnetic resonance spectrum (two bands at 1.73 τ to 2.01 τ and 2.26 τ to 2.51 τ). The infrared spectrum in carbon tetrachloride exhibited strong absorptions at 1 510, 1 483, 1 259, 1 192, and 1 010 cm^{-1}. Those at 1 510, 1 259, and

1 192 cm^{-1} were tentatively assigned to C=N, —S—S—, and C=S stretching vibrations, respectively. The peak at 1 010 cm^{-1} was probably similar to that found in the related 1,2-dithiole-3-thiones, which also exhibit strong absorptions in this region (11).

With methyl iodide, 5-phenyl-1,2,4-dithiazole-3-thione formed a violet 1:1 adduct which, by analogy with the corresponding derivatives of dithiolethiones, should be formulated as a 3-methylthio-1,2,4-dithiazolium iodide (VII). The infrared spectrum of a liquid paraffin mull of the adduct exhibited strong absorptions at 1 405, 1 340, 1 220, 1 049, 766, and 674 cm^{-1}. The proton magnetic resonance spectrum showed a singlet at 7.84 τ which was assigned to the protons on the the *S*-methyl group.

Like 1,2-dithiole-3-thiones (VI) (12), the 1,2,4-dithiazole-3-thiones formed adducts with activated acetylenes and with benzene. 5-Phenyl-1,2,4-dithiazole-3-thione reacted with dimethyl acetylenedicarboxylate, ethyl propiolate, and ethyl phenylpropiolate, and 5-(α-thienyl)-1,2,4-dithiazole-3-thione reacted with ethyl propiolate, to give high yields of substituted 2-thioacylimino-1,3-dithioles (VIII) by 1,3-dipolar cycloaddition reactions. Similarly, treatment with benzene (13) in boiling benzene gave the 4,5-benzo-1,3-dithiole derivative VIII*d*. In no case was any evidence obtained for the formation of di-adducts of the type obtained by Easton and Leaver for the dithiolethiones (12).

A proton magnetic resonance study of the ethyl ester VIII*a* and the methyl ester VIII*c* gave results in agreement with the proposed structures. Compound VIII*a* showed a triplet centered at 8.63 τ and a quartet centered at 5.65 τ characteristic of the ethyl group. The aromatic protons were evident as two bands at 1.51 τ to 1.71 τ and 2.48 τ to 2.79 τ. A sharp peak at 1.98 τ was assigned to the single vinyl proton. Compound VIII*c* exhibited one singlet at 6.04 τ assigned to the two methyl groups. Their equivalence is probably merely fortuitous. Two bands at 1.49 τ to 1.69 τ and 2.40 τ to 2.76 τ were assigned to the aromatic protons.

EXPERIMENTAL

Acyl Isothiocyanates

These were prepared by the method of Lipp *et al.* (6). The compounds were purified by fractional distillation under a reduced pressure.

Methyl N-Acylthionocarbamates

These were prepared from the appropriate isothiocyanates by treatment with methanol (cf. Skinner and Vogt (14)). The crude products were recrystallized from benzene.

Methyl N-Acyldithiocarbamates

The appropriate isothiocyanates were treated at 0° with an excess of methanethiol in a sealed flask. The mixtures became solid after several minutes. After 6 h the flasks were opened and the excess methanethiol was allowed to evaporate. The dithiocarbamates were recrystallized from benzene.

5-Aryl-1,2,4-dithiazole-3-thiones

Method A

The appropriate isothiocyanate (10 g) and phosphorus pentasulfide (20 g) in carbon disulfide (60 ml) were heated under reflux for times varying from 20 to 120 min. The solutions were filtered and evaporated under a reduced pressure. The oily residues were treated with ethanol (approximately 30 ml) and cooled to 0°. The crude thiones were filtered off and recrystallized from benzene–ethanol (1:1), except where stated. The results are presented in Table I. Although method A gave poorer results than method B, it was used for convenience in most of the preparations.

Method B

Methyl *N*-benzoyldithiocarbamate (5 g) and phosphorus pentasulfide (20 g) in benzene (40 ml) were refluxed for 2 h. The dark-red solution was worked up as in method A to yield 3.1 g (62%) of 5-phenyl-1,2,4-dithiazole-3-thione.

Method C

The appropriate thionocarbamate (5 g) was sulfurized as in method B. Evaporation yielded a dark-red oil, which gave 5-phenyl-1,2,4-dithiazole-3-thione (0.1 g), methyl benzoate, thiobenzamide, and sulfur when worked up.

Sulfurization of Cinnamoyl Isothiocyanate

The thiocyanate (10 g) was treated with phosphorus pentasulfide (20 g) in boiling carbon disulfide (50 ml) for 1.5 h. The orange solution was filtered and evaporated to a brownish solid, which recrystallized from ethanol as yellow plates, m.p. 123°.

Anal. Found: C, 53.7; H, 4.02; N, 6.27; S, 28.50. $C_{10}H_9NS_2O$ requires C, 53.49; H, 4.42; N, 6.38; S, 28.43.

Sulfurization of Methyl N-Cinnamoyldithiocarbamate

The reaction, performed as described for the other dithiocarbamates, gave only an uncrystallizable brown tar.

Sulfurization of Thiobenzoyl Isocyanate

Freshly prepared thiobenzoyl isocyanate (1 g) (10) was treated with phosphorus pentasulfide (5 g)

TABLE I

Preparation of 1,2,4-dithiazole-3-thiones from aroyl isothiocyanates

Compound	Reaction time (min)	Yield (%)	Melting point (°C)	Formula	Required (%)					Found (%)				
					C	H	N	S	Cl	C	H	N	S	Cl
III*a*	90	15	136*	$C_8H_5NS_3$	45.6	2.37	6.60	45.64		45.40	2.53	6.75	45.67	
III*b*	90	19	119	$C_9H_7NS_3$	48.23	3.13	6.23	42.70		48.34	3.10	6.23	42.80	
III*c*	90	14	94–95	$C_9H_7NS_3$	48.23	3.13	6.23	42.70		47.92	3.16	6.25	42.91	
III*d*	30	11	93	$C_{10}H_9NS_3$	50.20	3.77	5.89	40.22		49.91	3.75	5.89	41.44	
III*e*	30	10	103†	$C_9H_7NOS_3$	44.81	2.91	5.81	39.81		44.78	2.78	5.89	39.31	
III*f*	120	8	89–91‡	$C_8H_4ClNS_3$	39.10	1.59	5.70	39.11	14.40	38.75	1.66	5.61	38.6	14.60
III*g*	120	7	126§	$C_8H_4ClNS_3$	39.10	1.59	5.70	39.11	14.40	39.89	1.71	5.67	40.08	13.93
III*h*	20	23	164‖	$C_6H_3NS_4$	32.92	1.82	6.43	58.52		33.20	1.73	6.52	58.90	
III*i*	20	9	145¶	$C_6H_3NOS_3$	35.91	1.49	6.99	47.82		35.47	1.52	6.77	47.98	
III*j*	120	11	91**	$C_{12}H_7NS_3$	55.21	2.68	5.37	36.69		55.41	2.76	5.33	36.47	
III*k*	30	6	172	$C_{12}H_7NS_3$	55.21	2.68	5.37	36.69		55.41	2.87	5.56	36.61	

*Literature (5) m.p. 136 °C.
†Literature (5) m.p. 115 °C.
‡Literature (5) m.p. 98 °C.
§Literature (5) m.p. 137 °C.
‖Literature (5) m.p. 165 °C.
¶After a preliminary sublimation under a reduced pressure.
**Crystallized from nitromethane.

TABLE II

Preparation of 2-thioacylimino-1,3-dithioles from 1,2,4-dithiazole-3-thiones and acetylenic esters

Compound	Yield (%)	Melting point (%)	Formula	Required (%)				Found (%)			
				C	H	N	S	C	H	N	S
VII*a*	61	133	$C_{13}H_{11}NO_2S$	50.71	3.56	4.52	31.12	51.08	3.68	4.47	29.89
VII*b*	52	138	$C_{19}H_{15}NO_2S_3$	59.19	3.90	3.64	24.95	59.29	3.75	3.83	24.85
VII*c*	59	155	$C_{14}H_{11}NO_4S_3$	47.62	3.11	3.96	27.21	48.16	2.88	4.17	27.49
VII*d*	56	130	$C_{11}H_9NO_2S_4$	42.13	2.87	4.46	40.75	42.04	3.00	4.42	40.45

in boiling carbon disulfide (20 ml). The initially violet solution rapidly became brown (5 min). Only a tar was obtained when the mixture was worked up.

Sulfurization of 2-Phenyl-1,3-thiazoline-4,5-dione

The dione (2 g) prepared by the method of Goerdeler and Schenk (10) was treated with phosphorus pentasulfide (5 g) in boiling benzene (20 ml) for 1.5 h. The filtered solution, on evaporation, yielded pale-yellow plates, which were crystallized from ethanol, m.p. 75–80°.

Anal. Found: C, 46.81; H, 2.32; N, 6.64; S, 36.64.

Reaction of 5-Phenyl-1,2,4-dithiazole-3-thione with Ammonia

The thione (1 g) in ethanol (10 ml) was treated at the boiling point with a stream of ammonia until there was no further color change. The yellow solution, when cooled, deposited elemental sulfur (approximately 0.4 g), and when worked up gave thiobenzamide (0.3 g). Addition of ferric ion to the mother liquors produced no red coloration, indicating the absence of thiocyanate ion.

Reaction of 5-Phenyl-1,2-4-dithiazole-3-thione with Aniline

The thione (1.05 g) in ethanol (10 ml) was treated at the boiling point with aniline (0.45 g). The solution became yellow and, when cooled, gave elemental sulfur. Work-up yielded *N*-phenylthiobenzamide (0.42 g).

Thermal Decomposition of 5-Phenyl-1,2,4-dithiazole-3-thione

The thione (0.1 g) was heated gently in a sealed tube until complete decomposition was evident. Sulfur, carbon disulfide, and benzonitrile were identified by comparison of retention times on a gas chromatograph with authentic samples.

2-Thioacylimino-1,3-dithioles

The thiones III*a*–III*h* (0.5 g) were heated gently with acetylenic esters (1 g) until the mixture became homogeneous. Reaction was evident by the rapid color change from red brown to greenish red. After 5 min the mixtures were diluted with ethanol (1 ml) and allowed to cool. The adducts were collected and recrystallized from benzene or nitromethane. The results are presented in Table II.

2-Thiobenzoylimino-4,5-benzo-1,3-dithiole

To 5-phenyl-1,2,4-dithiazole-3-thione (1.05 g) and isoamyl nitrite (0.58 g) in boiling benzene (20 ml) was slowly added powdered anthranilic acid (0.7 g). The initially red-brown solution became greenish red. After 10 min the mixture was filtered and evaporated to 5 ml. The product was collected and recrystallized from benzene as green-yellow plates, m.p. 171 °C, yield 0.38 g (25%).

Anal. Found: C, 59.01; H, 2.95; N, 4.98; S, 33.43. $C_{14}H_9NS_3$ requires C, 58.6; H, 3.14; N, 4.89; S, 33.5.

Reaction of 5-Phenyl-1,2,4-dithiazole-3-thione with Methyl Iodide

The thione (1 g) was dissolved in methyl iodide, and the mixture was allowed to stand for 16 h. The mixture was filtered to give dark-violet needles, which slowly decomposed above 90°. They could not be crystallized satisfactorily from any solvent.

Anal. Found: C, 30.53; H, 2.14; N, 3.92; S, 27.11; I, 36.23. $C_9H_8NS_3I$ requires C, 30.55; H, 2.26; N, 3.96; S, 27.1; I, 35.9.

REFERENCES

1. E. Fromm. Ann. **275**, 20 (1893).
2. R. E. Allen, R. S. Shelton, and M. G. VanCampen. J. Am. Chem. Soc. **76**, 1158 (1954).
3. H. J. Emeléus, A. Haas, and N. Sheppard. J. Chem. Soc. 3165 (1963).
4. H. Behringer and D. Weber. Ber. **97**, 2567 (1964).
5. J. Derocque and J. Viaille. Bull. Soc. Chim. France, 1183 (1966).
6. T. B. Johnson and L. H. Chernoff. J. Am. Chem. Soc. **33**, 167 (1912). M. Lipp, F. Dallacker, and G. Koener. Ber. **91**, 1160 (1958).
7. D. T. Elmore, J. R. Ogle, W. Fletcher, and P. A. Toseland. J. Chem. Soc. 4458 (1956).
8. B. H. Nicolet. J. Am. Chem. Soc. **53**, 3066 (1931); **57**, 1098 (1935).
9. J. E. Jansen. Chem. Abstr. **46**, 3574 (1952).
10. J. Goerdeler and H. Schenk. Ber. **98**, 2962 (1965).
11. J. Fabian and R. Mayer. Chem. Ind. London, 1962 (1966).
12. H. Behringer and R. Wiedenmann. Tetrahedron Letters, 3705 (1965). D. B. J. Easton and D. Leaver. Chem. Commun. 585 (1965).
13. L. Friedman and F. M. Logullo. J. Am. Chem. Soc. **85**, 1549 (1963).
14. G. S. Skinner and H. C. Vogt. J. Am. Chem. Soc. **77**, 5440 (1955).