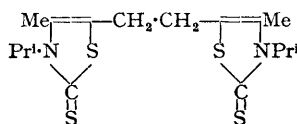


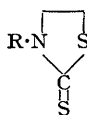
the exocyclic (II) to the cyclic (IV) position, and this conclusion was confirmed by the fact that light-absorption properties of the rearranged products were in good agreement with those of 4-methyl-3-isopropylthiazole-2-thione (VI; $R = \text{Pr}^i$) which was synthesised from chloroacetone and isopropylammonium isopropylthiocarbamate (V; $R = \text{Pr}^i$). The rearranged products (IV) were finally proved to be 3-alkyl-4:5-dimethylthiazole-2-thiones by the synthesis of (IV; $R = \text{Pr}^i$ and *cyclo*- C_6H_{11}) from 3-bromobutan-2-one and the appropriate dithiocarbamate (V; $R = \text{Pr}^i$ and *cyclo*- C_6H_{11}). That these condensations did not occur by an initial dehydrobromination followed by an addition to the terminal carbon atom of methyl vinyl ketone was shown by the fact that methyl 2-chloroethyl ketone and (V; $R = \text{Pr}^i$) gave (84%) 3-ketobutyl N-isopropylthiocarbamate (VII; $R = \text{Pr}^i$) which was decomposed and not cyclised by treatment with cold concentrated sulphuric acid or by being heated in alcoholic solution.

The rearrangement also occurred when (II; $R = \text{cyclohexyl}$) was heated with either concentrated hydrochloric acid or alcoholic sodium ethoxide but not with pyridine or piperidine.

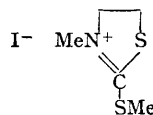
2:6-Diisopropylaminoocta-3:5-diyne and alcoholic carbon disulphide gave a high-melting solid which exhibited characteristic light absorption and was recovered unchanged after treatment with cold concentrated sulphuric acid. The structure (IX) is tentatively proposed for this product.



(IX.)

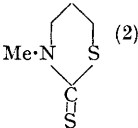


(VIII.)



(X.)

Treatment of the primary condensation product (II; $R = \text{cyclo-C}_6\text{H}_{11}$) with Raney nickel gave a sulphur-free base, the methiodide of which was undepressed on admixture with that of cyclohexylmethyl-sec.-butylamine, which was synthesised from 2-cyclohexylaminobut-3-yne (I; $R = \text{C}_6\text{H}_{11}$) by hydrogenation to cyclohexyl-sec.-butylamine followed by alkylation with methyl iodide.

	$\lambda_{\text{max.}}$ A.	$\epsilon_{\text{max.}}$		$\lambda_{\text{max.}}$ A.	$\epsilon_{\text{max.}}$
$\text{Me}_2\text{N}\cdot\text{CS}\cdot\text{SMe}$ (1)	2760	10,000	II; $R = \text{Pr}^i$	2770	16,000
	2460	8,000		ca. 3200 *	270
VII; $R = \text{Pr}^i$	2735	9,500	II; $R = \text{Bu}^n$	2770	17,000
	2540	9,500		3210	2,000
	2190	8,000	II; $R = \text{cyclo-C}_6\text{H}_{11}$...	2810	17,500
			II; $R = \text{Ph}\cdot\text{CH}_2$	2800	19,000
 (2)	2825	—	VI; $R = \text{Pr}^i$	3225	12,500
				2485	2,200
VIII; $R = \text{Me}$	2700	17,000	IV; $R = \text{Pr}^i$	3240	13,500
VIII; $R = \text{Bu}^n$	2700	17,000		2360	2,700
			IV; $R = \text{Bu}^n$	3245	13,000
				2325 *	2,600
			IV; $R = \text{cyclo-C}_6\text{H}_{11}$	3230	13,000
			IV; $R = \text{Ph}\cdot\text{CH}_2$	3240	12,000
			IX	3240 †	37,000
				2750	25,500

* Inflexion.

† In chloroform.

(1) Ainley, Davies, Gudgeon, Harland, and Sexton, *J.*, 1944, 147 (in cyclohexane).(2) Hamer and Rathbone, *J.*, 1943, 243.

3-Methylthiazolidine-2-thione (VIII; $R = \text{Me}$) reacted readily with methyl iodide giving 2-methylthiothiazoline methiodide (X).

EXPERIMENTAL.

(All absorption spectra were determined in methanol solution unless otherwise stated.)

4-Methyl-3-isopropyl-5-methylenethiazolidine-2-thione (II; $R = \text{Pr}^i$).—(a) Carbon disulphide (10 c.c.) was added dropwise during 1 hour to a well-stirred mixture of sodium hydroxide (4 g.), water (30 c.c.), and 2-isopropylaminobut-3-yne (11.1 g.) at 50°. Stirring was continued for a further 2 hours, and the mixture was then cooled and the water-insoluble layer extracted with ether. Evaporation of the ethereal solution and distillation of the residue gave 4-methyl-3-isopropyl-5-methylenethiazolidine-2-thione (10.8 g.) as an oil, b. p. 130—135°/0.4 mm., which solidified and was crystallised from light petroleum (b. p. 40—60°) giving colourless prisms, m. p. 43° (Found: C, 51.05; H, 6.3; N, 7.5; S, 34.0. $\text{C}_8\text{H}_{13}\text{NS}_2$ requires C, 51.3; H, 6.95; N, 7.5; S, 34.2%).

(b) A solution of 2-isopropylaminobut-3-yne (10.6 g.) and carbon disulphide (10 c.c.) in alcohol (50 c.c.) was refluxed for 4 hours, cooled, and then evaporated under reduced pressure. Distillation of the residue gave the thione (8 g.), b. p. 110–120°/0.1 mm., which solidified on standing, m. p. and mixed m. p. with specimen from (a) 43°.

Ozonolysis. A solution of the thione (500 mg.) in "AnalaR" acetic acid (12 c.c.) was treated with a stream of ozonised oxygen (3%) at 20° until ozone was passing freely through the solution (2 hours). Zinc dust (500 mg.) was added, and the solution distilled in steam in an atmosphere of nitrogen. The distillate was neutralised with 2N-sodium hydroxide and treated with excess of "dimedone" in 10% methyl alcohol. The mixture was boiled under reflux for 10 minutes and cooled, and the precipitate collected and weighed; yield 160 mg., m. p. 189°, undepressed by admixture with an authentic specimen of formaldehyde "dimedone."

4-Methyl-3-n-butyl-5-methylenethiazolidine-2-thione (II; R = Buⁿ).—The reaction (a) above was repeated using 2-n-butylaminobut-3-yne (12.5 g.) in place of the isopropyl analogue, giving 4-methyl-3-n-butyl-5-methylenethiazolidine-2-thione (17.4 g.) as an oil, b. p. 140–142°/0.5 mm., n_D^{20} 1.5975 (Found: C, 53.8; H, 7.3; N, 6.8; S, 31.6. C₉H₁₅NS₂ requires C, 53.7; H, 7.5; N, 6.95; S, 31.85).

3-cyclohexyl-4-methyl-5-methylenethiazolidine-2-thione (II; R = C₆H₁₁).—(a) Carbon disulphide (20 c.c.) was added during 0.5 hour to 2-cyclohexylaminobut-3-yne (30 g.), sodium hydroxide (8 g.), and water (60 c.c.), and the mixture stirred at 50° for 4 hours. Isolation of the water-insoluble layer gave (i) recovered aminobut-3-yne (5 g.), and (ii) 3-cyclohexyl-4-methyl-5-methylenethiazolidine-2-thione (26 g.) as an oil, b. p. 150–160°/0.15 mm., which solidified and was recrystallised from light petroleum (b. p. 40–60°), giving colourless prisms, m. p. 69–70° (Found: N, 6.35; S, 28.0. C₁₁H₁₈NS₂ requires N, 6.1; S, 27.95%).

(b) A solution of 2-cyclohexylaminobut-3-yne (15 g.) and carbon disulphide (10 c.c.) in alcohol (30 c.c.) was refluxed for 4 hours and then evaporated under reduced pressure. Distillation of the residue gave (i) recovered aminobut-3-yne (5.5 g.), and (ii) the thione (7 g.), b. p. 150–160°/0.15 mm., which solidified and after crystallisation from light petroleum (b. p. 40–60°) had m. p. 69°, undepressed on admixture with a specimen from (a).

3-Benzyl-4-methyl-5-methylenethiazolidine-2-thione (II; R = Ph·CH₂).—A solution of 2-benzylaminobut-3-yne (10 g.) and carbon disulphide (10 c.c.) in alcohol (40 c.c.) was refluxed for 6 hours and then evaporated under reduced pressure. Distillation of the residue gave 3-benzyl-4-methyl-5-methylenethiazolidine-2-thione (12 g.) as a pale yellow oil, b. p. 165–175°/0.075 mm. (Found: C, 61.45; H, 5.1; N, 6.2; S, 27.65. C₁₅H₁₃NS₂ requires C, 61.3; H, 5.5; N, 5.95; S, 27.25%).

1:2-Di-(4'-methyl-3'-isopropyl-2'-thion-5'-thiazolyl)ethane (IX).—A solution of 2:7-diisopropylamino-octa-3:5-diyne (5 g.) and carbon disulphide (3 c.c.) in ethanol (30 c.c.) was refluxed for 4 hours, during which time a solid was deposited. After cooling the solid was filtered off and recrystallised from pyridine, giving 1:2-di-(4'-methyl-3'-isopropyl-2'-thion-5'-thiazolyl)ethane (2.5 g.) as needles, m. p. 270° (decomp.) (Found: C, 51.5; H, 6.4; N, 7.6; S, 34.85. C₁₆H₂₄N₂S₄ requires C, 51.6; H, 6.45; N, 7.5; S, 34.4%).

4:5-Dimethyl-3-isopropylthiazole-2-thione (IV; R = Prⁿ).—(a) 4-Methyl-3-isopropyl-5-methylene-thiazolidine-2-thione (2.5 g.) was dissolved in cold concentrated sulphuric acid (10 c.c.) and the solution poured on crushed ice. The precipitated solid was recrystallised from aqueous methanol, giving 4:5-dimethyl-3-isopropylthiazole-2-thione (2 g.) as colourless needles, m. p. 84–86° (Found: C, 51.1; H, 6.95; N, 7.9; S, 34.25. C₈H₁₃NS₂ requires C, 51.3; H, 6.95; N, 7.5; S, 34.2%).

(b) A solution of carbon disulphide (4.85 g.) in alcohol (10 c.c.) was added slowly to a well-stirred solution of isopropylamine (7.5 g.) in alcohol (15 c.c.). To the resulting suspension of dithiocarbamate, 3-bromobutan-2-one (9 g., Faworsky, *J. pr. Chem.*, 1913, **88**, 657) was added slowly (0.5 hour). The solution was then refluxed for 0.5 hour, cooled, and poured into water (500 c.c.). Extraction with ether and evaporation of the ethereal solution gave a viscous oil which was dissolved in concentrated sulphuric acid (40 c.c.) with cooling in an ice-bath. The acid solution was poured on crushed ice, and the precipitated solid filtered off and recrystallised from aqueous methanol, giving the thione (7.2 g.) as colourless needles, m. p. 84–85° undepressed on admixture with a specimen from (a). Ozonisation of the dimethyl-isopropylthiazole-2-thione, as described above for the unrearranged isomer, gave no formaldehyde.

4:5-Dimethyl-3-n-butylthiazole-2-thione (IV; R = Buⁿ).—A solution of 4-methyl-3-n-butyl-5-methylenethiazolidine-2-thione (5 g.) in concentrated sulphuric acid (15 c.c.) was poured on crushed ice. The precipitated oil slowly solidified, giving 4:5-dimethyl-3-n-butylthiazole-2-thione (4.3 g.) which crystallised from aqueous methanol or from ether as pale yellow prisms, m. p. 42–44° (Found: C, 53.7; H, 7.25; N, 6.8; S, 31.8. C₉H₁₅NS₂ requires C, 53.17; H, 7.15; N, 6.95; S, 31.85%).

3-cyclohexyl-4:5-dimethylthiazole-2-thione (IV; R = cyclo-C₆H₁₁).—(a) A solution of 3-cyclohexyl-4-methyl-5-methylenethiazolidine-2-thione (2 g.) in concentrated sulphuric acid (10 c.c.) was poured on crushed ice, and the precipitated solid recrystallised from methanol, giving 3-cyclohexyl-4:5-dimethylthiazole-2-thione (1.8 g.) as colourless needles, m. p. 104° (Found: N, 6.15; S, 28.1. C₁₁H₁₉NS₂ requires N, 6.1; S, 27.95%).

(b) A solution of carbon disulphide (4.3 g.) in alcohol (10 c.c.) was added slowly with stirring to cyclohexylamine (11 g.) in alcohol (40 c.c.). To the suspension of dithiocarbamate thus obtained 3-bromobutan-2-one (8.3 g.) was added during 0.5 hour, and the resulting solution refluxed for 0.5 hour, cooled, and poured into water (500 c.c.). Isolation of the product as in the case of the 3-isopropyl analogue gave the thione (8 g.) which crystallised in needles from methanol, m. p. 104°, undepressed on admixture with a specimen from (a).

3-Benzyl-4:5-dimethylthiazole-2-thione (IV; R = Ph·CH₂).—A solution of 3-benzyl-4-methyl-5-methylenethiazolidine-2-thione (2 g.) in concentrated sulphuric acid (10 c.c.) was poured on ice. The dilute acid was decanted from the precipitated gum and the latter triturated with methanol. The resulting solid was recrystallised from the same solvent giving 3-benzyl-4:5-dimethylthiazole-2-thione (1.7 g.) as prisms, m. p. 111° (Found: C, 61.3; H, 5.5; N, 5.9; S, 27.5. C₁₂H₁₃NS₂ requires C, 61.3; H, 5.5; N, 5.9; S, 27.25%).

4-Methyl-3-isopropylthiazole-2-thione (VI; R = Prⁿ).—Carbon disulphide (19.5 g.) was added slowly to a solution of isopropylamine (30 g.) in alcohol (100 c.c.). To the resulting dithiocarbamate suspension,

chloroacetone (23 g.) was added during 0·5 hour. After being boiled under reflux for 0·5 hour, the solution was evaporated under reduced pressure, and water (500 c.c.) added to the viscous residue. The insoluble fraction was extracted with ether. Evaporation of the ethereal solution gave 4-methyl-3-isopropylthiazole-2-thione (26 g.) which crystallised in plates from aqueous methanol, or needles from light petroleum (b. p. 60—80°), m. p. 68—69° (Found: C, 48·45; H, 6·25; N, 8·45; S, 36·85. $C_7H_{11}NS_2$ requires C, 48·5; H, 6·35; N, 8·1; S, 37·0%).

3-Ketobutyl N-isoPropylthiocarbamate (VII; R = Prt).—Carbon disulphide (9·7 g.) was added to a well-stirred solution of isopropylamine (15 g.) in alcohol (50 c.c.). To the resulting suspension, methyl 2-chloroethyl ketone (13 g.; Scheller and Zellner, U.S.P. 1,737,203) was added during 0·5 hour, and the solution was left at room temperature for 2 days and then poured into water (500 c.c.). Extraction with ether and evaporation of the ethereal solution gave 3-ketobutyl N-isoPropylthiocarbamate (21 g.) which crystallised from light petroleum (b. p. 60—80°) in plates, m. p. 62° (Found: C, 46·8; H, 7·05; N, 6·95; S, 31·3. $C_8H_{15}ONS_2$ requires C, 46·8; H, 7·35; N, 6·8; S, 31·25%).

cycloHexyl-sec-butylamine.—A solution of 2-cyclohexylaminobut-3-yne (20 g.) in methanol (75 c.c.) was shaken with hydrogen (100 atm.) and Raney nickel until absorption was complete. After filtration, the solution was acidified with concentrated hydrochloric acid and evaporated to dryness under reduced pressure. The solid hydrochloride thus obtained was treated with excess of sodium hydroxide solution (20%) and the free base isolated. Distillation gave cyclohexyl-sec-butylamine (15 g.) as a colourless liquid, b. p. 86—88°/25 mm., n_D^{20} 1·4350 (Found: C, 77·2; H, 13·15; N, 9·15. $C_{10}H_{21}N$ requires C, 77·4; H, 13·5; N, 9·0%). The hydrochloride crystallised in needles from aqueous acetone, m. p. 210° (Found: C, 62·65; H, 11·2; N, 7·6. $C_{10}H_{21}N \cdot HCl$ requires C, 62·65; H, 11·4; N, 7·3%).

cycloHexylmethyl-sec-butylamine.—(a) Methyl iodide (9 g.) was added to a mixture of cyclohexyl-sec-butylamine (10 g.) and powdered potassium hydroxide (5 g.). After being heated for 2 hours on the steam-bath, the mixture was cooled and treated with excess of aqueous sodium hydroxide solution (20%). The base was isolated, dissolved in dilute hydrochloric acid, and treated with a slight excess of saturated sodium nitrite solution. The precipitated oil was extracted with ether, and the tertiary base liberated from the aqueous solution by adding excess of sodium hydroxide solution. Isolation of the base gave cyclohexylmethyl-sec-butylamine (4·5 g.) as a colourless liquid, b. p. 90—93°/22 mm. The methiodide crystallised from alcohol-ether in needles, m. p. 174—176° (Found: C, 46·55; H, 8·2; N, 4·05. $C_{12}H_{23}NI$ requires C, 46·3; H, 8·3; N, 4·3%).

(b) A suspension of Raney nickel (20 c.c.) in alcohol was added to a solution of 3-cyclohexyl-4-methyl-5-methylenethiazolidine-2-thione (3 g.) in alcohol (80 c.c.), and the mixture refluxed for 4 hours. The basic fraction (0·4 g.) was isolated and converted into the methiodide, which after repeated crystallisation from alcohol-ether had m. p. 170° undepressed on admixture with a specimen from (a).

3-Methylthiazolidine-2-thione (VIII; R = Me).—A solution of 2-methylaminoethanol (5 g.) in carbon disulphide (7 c.c.) was heated in a steel autoclave at 120—140° for 3·5 hours. After cooling, the crude product was dissolved in chloroform and the solution washed well with water, dried, and evaporated. Distillation of the residue gave an oil (5·8 g.), b. p. 90—100° (bath temp.)/10⁻⁴ mm., which solidified on cooling and was recrystallised from benzene-cyclohexane, giving 3-methylthiazolidine-2-thione as colourless needles, m. p. 68—69° (Found: C, 36·1; H, 5·25; N, 10·75. $C_4H_7NS_2$ requires C, 36·05; H, 5·3; N, 10·5%).

2-Methylthiothiazoline Methiodide (X).—3-Methylthiazolidine-2-thione (1·8 g.) was dissolved in methyl iodide (1·5 c.c.). Heat was evolved, and the mixture, which was cooled to prevent the temperature from rising above 40°, solidified. The crude product was crystallised from ethanol, giving 2-methylthiothiazoline methiodide (3·2 g.) as colourless leaflets, m. p. 132° (sinters at 125°) (Found: C, 22·05; H, 3·8; N, 4·85. $C_5H_9NS_2I$ requires C, 21·9; H, 3·3; N, 5·1%).

3-n-Butylthiazolidine-2-thione (VIII; R = Buⁿ).—A solution of 2-n-butylaminoethanol (5 g.) in carbon disulphide (5 c.c.) was heated in a steel autoclave at 120—140° for 3·5 hours. After cooling, the contents of the autoclave were poured into water and the product isolated by extraction with ether. Distillation of the residue after evaporation of the ethereal solution gave 3-n-butylthiazolidine-2-thione (4·9 g.) as a yellow oil, b. p. 90—95° (bath temp.)/10⁻⁴ mm., n_D^{25} 1·5970 (Found: C, 47·75; H, 7·35; N, 8·0. $C_7H_{13}NS_2$ requires, C, 48·0; H, 7·5; N, 8·0%).

The authors wish to thank Mr. J. D. Rose for his advice and encouragement in this work.

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[Received, September 3rd, 1948.]