168. *Acetylene Reactions. Part III. Reaction of Aminobutynes with Carbon Disulphide.*

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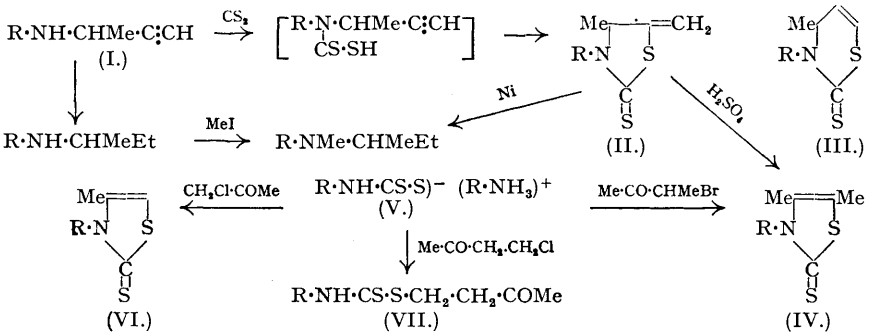
Monoalkylaminobutynes (I) and carbon disulphide react readily to give 4-methyl-3-alkyl-5-methylenethiazolidine-2-thiones (II). These, on treatment with concentrated sulphuric acid, are isomerised to 4 : 5-dimethyl-3-alkylthiazol-2-thiones.

In attempting to prepare the sodium dithiocarbamate of 3-*iso*propylaminobut-1-yne (I; R = Pr^i), a neutral product was obtained in 58% yield by condensation of the amine and carbon disulphide in equimolecular proportion, the reaction being carried out in the presence of aqueous sodium hydroxide. The aminobutynes (I; R = Bu^n and *cyclo*-C_6H_{11}) gave the corresponding *n*-butyl-(87%) and *cyclo*hexyl-(70%) analogues. These reactions are thought to be similar to those which have been described between α-amino-nitriles and carbon disulphide giving mercaptothiazoles (Cook, Heilbron, and Levy, *J.*, 1947, 1598; 1948, 201), and the products from the aminobutynes have therefore been assigned the thiazolidine formulæ (II).



The alternative structure (III), which would result from an " abnormal " (anti-Markownikoff) internal addition of the intermediate dithiocarbamic acid to the triple linkage, was an obvious possibility, as such abnormal additions have been described; Kohler and Potter (*J. Amer. Chem. Soc.*, 1935, **57**, 1316) reported that phenylacetylene and thio-*p*-cresol give a β-substituted styrene derivative, and the " abnormal " addition of thiolacetic acid to acetylenes has been described by Bader, Cross, Heilbron, and Jones (this vol., p. 619).

The presence of the methylene group in (II), the thiazolidine structure of which was confirmed by other evidence given later in the paper, was established by ozonolysis to formaldehyde, and the infra-red spectrum of (II; R = Pr^i) which exhibits a fairly strong absorption band at *ca.* 875 cm.$^{-1}$ [this band is not observed in the spectra of (IV; R = Pr^i) and (VI; R = Pr^i)]. An absorption band at 870—910 cm.$^{-1}$ occurs in compounds containing the grouping $R_1R_2C{:}CH_2$ (Thompson, *J.*, 1948, 328; Barnes, Gore, Stafford, and Williams, *Anal. Chem.*, 1948, **20**, 402).

The only previously recorded example of the reaction of an acetylenic amine with carbon disulphide is that of propargylamine in alcoholic solution (Paal and Heupel, *Ber.*, 1891, **24**, 3041); the product was described as the corresponding acetylenic dithiocarbamic acid, but a consideration of its mode of formation and properties makes it virtually certain that these authors had, in fact, prepared the parent member of this series, the isomeric 5-methylenethiazolidine-2-thione. Under similar conditions, the monoalkylaminobutynes (I), referred to above, all gave products which were identical with those prepared in the presence of aqueous sodium hydroxide. Benzylaminobutyne (I; R = Ph·CH_2) also gave an 81% yield of the required product, but anilinobutyne (I; R = Ph) did not react.

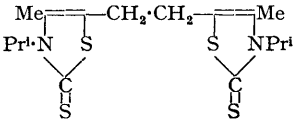
The products (II) from the monoalkylaminobutynes all exhibited ultra-violet light absorption (see Table) similar to that of 3-*methyl*- and 3-n-*butyl-thiazolidine*-2-*thione* (VIII; R = Me and Bu^n), which were synthesised by heating the appropriate β-alkylamino-ethanol with carbon disulphide (cf. the powerful chromolatory effect of the sulphur atom in the chromophore $CH{:}CH{\cdot}S{\cdot}CO{\cdot}CH_3$, Bader, Cross, Heilbron, and Jones, *loc. cit.*).

The primary condensation products (II) were readily rearranged by cold concentrated sulphuric acid, giving (80—90% yield) isomeric compounds (IV) which showed maximal light absorption at wave-lengths between 420 and 470 A. longer than those shown by the starting materials (II). The results were interpreted as indicating a migration of the double bond from

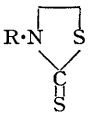
the exocyclic (II) to the cyclic (IV) position, and this conclusion was confirmed by the fact that light-absorption properties of the rearranged products were in good agreement with those of 4-*methyl*-3-iso*propylthiazole*-2-*thione* (VI; R = Pr^i) which was synthesised from chloroacetone and *iso*propylammonium *iso*propyldithiocarbamate (V; R = Pr^i). The rearranged products (IV) were finally proved to be 3-*alkyl*-4 : 5-*dimethylthiazole*-2-*thiones* by the synthesis of (IV; R = Pr^i and *cyclo*-C_6H_{11}) from 3-bromobutan-2-one and the appropriate dithiocarbamate (V; R = 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 = Pr^i) gave (84%) 3-*ketobutyl* N-iso*propyldithiocarbamate* (VII; R = 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 = *cyclo*hexyl) was heated with either concentrated hydrochloric acid or alcoholic sodium ethoxide but not with pyridine or piperidine.

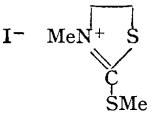
2 : 6-Di*iso*propylaminoocta-3 : 5-diyne and alcoholic carbon disulphide gave a high-melting solid which exhibited characteristic light absorption and was recovered unchanged after treatment with cold concentrated sulphuric acid. The structure (IX) is tentatively proposed for this product.



(IX.)

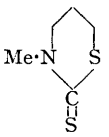


(VIII.)



(X.)

Treatment of the primary condensation product (II; R = *cyclo*-C_6H_{11}) with Raney nickel gave a sulphur-free base, the methiodide of which was undepressed on admixture with that of cyclo*hexylmethyl*-sec.-*butylamine*, which was synthesised from 2-*cyclo*hexylaminobut-3-yne (I; R = C_6H_{11}) by hydrogenation to cyclo*hexyl*-sec.-*butylamine* followed by alkylation with methyl iodide.

	$\lambda_{max.}$ A.	$\varepsilon_{max.}$
$Me_2N{\cdot}CS{\cdot}SMe$ (1)	2760	10,000
	2460	8,000
VII; R = Pr^i	2735	9,500
	2540	9,500
	2190	8,000
 (2)	2825	—
VIII; R = Me	2700	17,000
VIII; R = Bu^n	2700	17,000

	$\lambda_{max.}$ A.	$\varepsilon_{max.}$
II; R = Pr^i	2770	16,000
	ca. 3200 *	270
II; R = Bu^n	2770	17,000
	3210	2,000
II; R = *cyclo*-C_6H_{11} ...	2810	17,500
II; R = Ph·CH_2	2800	19,000
VI; R = Pr^i	3225	12,500
	2485	2,200
IV; R = Pr^i	3240	13,500
	2360	2,700
IV; R = Bu^n	3245	13,000
	2325 *	2,600
IV; R = *cyclo*-C_6H_{11}	3230	13,000
IV; R = Ph·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 *cyclo*hexane).
(2) Hamer and Rathbone, *J.*, 1943, 243.

3-Methylthiazolidine-2-thione (VIII; R = 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-iso*propyl*-5-*methylenethiazolidine*-2-*thione* (II; R = 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-*iso*propylaminobut-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-iso*propyl*-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. $C_8H_{13}NS_2$ requires C, 51·3; H, 6·95; N, 7·5; S, 34·2%).

(*b*) A solution of 2-*iso*propylaminobut-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 = Bu^n).—The reaction (*a*) above was repeated using 2-*n*-butylaminobut-3-yne (12·5 g.) in place of the *iso*propyl analogue, giving 4-*methyl*-3-n-*butyl*-5-*methylenethiazolidine*-2-*thione* (17·4 g.) as an oil, b. p. 140—142°/0·5 mm., $n_D^{16°}$ 1·5975 (Found: C, 53·8; H, 7·3; N, 6·8; S, 31·6. $C_9H_{15}NS_2$ requires C, 53·7; H, 7·5; N, 6·95; S, 31·85).

3-cyclo*Hexyl*-4-*methyl*-5-*methylenethiazolidine*-2-*thione* (II; R = C_6H_{11}).—(*a*) Carbon disulphide (20 c.c.) was added during 0·5 hour to 2-*cyclo*hexylaminobut-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 aminobutyne (5 g.), and (ii) 3-cyclo*hexyl*-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. $C_{11}H_{19}NS_2$ requires N, 6·1; S, 27·95%).

(*b*) A solution of 2-*cyclo*hexylaminobut-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 aminobutyne (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·CH$_2$).—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*-3-*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. $C_{12}H_{13}NS_2$ requires C, 61·3; H, 5·5; N, 5·95; S, 27·25%).

1 : 2-*Di*-(4′-*methyl*-3′-iso*propyl*-2′-*thion*-5′-*thiazolyl*)*ethane* (IX).—A solution of 2 : 7-di*iso*propylamino-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′-iso*propyl*-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. $C_{16}H_{24}N_2S_4$ requires C, 51·6; H, 6·45; N, 7·5; S, 34·4%).

4 : 5-*Dimethyl*-3-iso*propylthiazole*-2-*thione* (IV; R = Pr^i).—(*a*) 4-Methyl-3-*iso*propyl-5-methylenethiazolidine-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-iso*propylthiazole*-2-*thione* (2 g.) as colourless needles, m. p. 84—86° (Found: C, 51·1; H, 6·95; N, 7·9; S, 34·25. $C_8H_{13}NS_2$ 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 *iso*propylamine (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-*iso*propylthiazole-2-thione, as described above for the unrearranged isomer, gave no formaldehyde.

4 : 5-*Dimethyl*-3-n-*butylthiazole*-2-*thione* (IV; R = Bu^n).—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. $C_9H_{15}NS_2$ requires C, 53·17; H, 7·15; N, 6·95; S, 31·85%).

3-cyclo*Hexyl*-4 : 5-*dimethylthiazole*-2-*thione* (IV; R = *cyclo*-C_6H_{11}).—(*a*) A solution of 3-*cyclo*hexyl-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-cyclo*hexyl*-4 : 5-*dimethylthiazole*-2-*thione* (1·8 g.) as colourless needles, m. p. 104° (Found: N, 6·15; S, 28·1. $C_{11}H_{19}NS_2$ 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 *cyclo*hexylamine (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-*iso*propyl 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·CH$_2$).—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. $C_{12}H_{13}NS_2$ requires C, 61·3; H, 5·5; N, 5·9; S, 27·25%).

4-*Methyl*-3-iso*propylthiazole*-2-*thione* (VI; R = Pr^i).—Carbon disulphide (19·5 g.) was added slowly to a solution of *iso*propylamine (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-iso*propyl*-*thiazole*-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-iso*Propyldithiocarbamate* (VII; R = Pr^i).—Carbon disulphide (9·7 g.) was added to a well-stirred solution of *iso*propylamine (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-iso*propyldithiocarbamate* (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%.

cyclo*Hexyl*-sec.-*butylamine*.—A solution of 2-*cyclo*hexylaminobut-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 cyclo*hexyl*-sec.-*butylamine* (15 g.) as a colourless liquid, b. p. 86—88°/25 mm., $n_D^{16°}$ 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. $C_{10}H_{21}N$,HCl requires C, 62·65; H, 11·4; N, 7·3%).

cyclo*Hexylmethyl*-sec.-*butylamine*.—(*a*) Methyl iodide (9 g.) was added to a mixture of *cyclo*hexyl-*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 *cyclo*hexylmethyl-*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. $C_{12}H_{26}NI$ 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-*cyclo*hexyl-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–*cyclo*hexane, 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-*methylthio*-*thiazoline 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 = Bu^n).—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., $n_D^{22·5°}$ 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%).

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