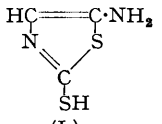
495. *Studies in the Azole Series. Part XXI. Experiments with N-Alkylamino-nitriles.*

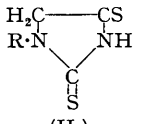
By A. H. Cook and S. F. Cox.

N-Alkylamino-nitriles react with carbon disulphide at rates depending on the substitution on the nitrogen and α-carbon atoms, the products being 5-amino-2-thio-3-alkylthiazolines. The behaviour of representative compounds towards methyl iodide, acid, and alkali is described.

In Part III of this Series (*J.*, 1948, 201) it was shown that the reaction between aminoacetonitrile and carbon disulphide led to the formation of 5-amino-2-mercaptothiazole (I) which was converted by alkali into 2 : 4-dithiohydantoin (II; R = H) and by acid into 2-mercapto-thiazol-5-one (III). It seemed likely that certain of the properties of these and related compounds might be due to the existence of a thiol group in the 2-position and it was decided to study substances in which this structure was precluded by the presence of an alkyl group on the adjacent nitrogen atom, *e.g.*, (IV). This work also forms part of a large study of *N*-alkyl-amino-acids and their derivatives prompted by the occurrence of related compounds in certain antibiotics (Cook and Cox, this vol., p. 2347).

The initial experiments were directed towards the preparation of 5-amino-2-thio-3-methyl-thiazoline (IV; R = H) by interaction of carbon disulphide with methylaminoacetonitrile. This is stated (U.S.P. 2,143,816) to lead to the formation of 1-methyl-2 : 4-dithiohydantoin (II; R = Me), but it was considered that the conditions used in the isolation of this material (extraction with alkali) might have led to secondary changes and that the aminothiazolone might be the first product (cf. Part III, *loc. cit.*, and Carrington, *J.*, 1948, 1620). When the two


(I.)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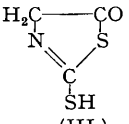
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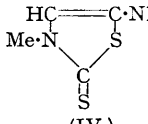
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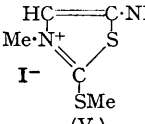
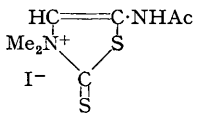

(V.)

compounds were mixed in solution, a vigorous reaction took place but the product was obtained as a gum which darkened rapidly on exposure to air or on warming it in solution. On treatment with acetic anhydride, it formed a stable crystalline derivative which yielded carbon disulphide on being heated under reflux with acid and so was formulated as *5-acetamido-2-thio-3-methyl-thiazoline* (IV; R = Ac). When the initial condensation was carried out in the presence of benzaldehyde, the Schiff's *base* of the aminothiazolone was formed. The acetyl derivative was remarkable for its ready solubility in sodium hydroxide from which it could be recovered unchanged, and an unsuccessful attempt was made to locate the active hydrogen atom by treatment with diazomethane. However, when the potassium salt was treated with methyl iodide in dry acetone, potassium iodide separated and a water-soluble product was formed. This must be considered as being a quaternary hydroxide as, on addition of hydrogen iodide, the corresponding *methiodide* was obtained; this could also be prepared directly from (IV; R = Ac) by boiling it with methyl iodide. Two structures, (V; R = Ac) and (VI), were possible for this compound, of which the first proved to be correct. Thus, on boiling it with alkali, methyl thiol was evolved, and in hot mineral acid an acid material was formed which was shown to be N-*dithiocarbomethoxy*-N-*methylglycine* (VII; R = Me, R′ = OH) by its synthesis from sarcosine and carbon disulphide by the method of Körner (*Ber.*, 1908, **41**, 1901). The possibility that the methyl group might have wandered under the conditions of hydrolysis was disproved by the synthesis of (V; R = Ac) by an alternative route. 5-Acetamido-2-mercaptothiazole (VIII; R = H) was treated with methyl iodide, giving the *hydriodide* of 5-acetamido-2-methyl-thiothiazole (VIII; R = Me). This dissolved in sodium hydroxide but, on addition of acetic

acid, the free *base* was liberated which reacted further with methyl iodide to give a product identical with that already obtained.

Initial attempts to prepare 2-thio-3-methylthiazolid-5-one (IX) were made by using the method which had proved most satisfactory with the unsubstituted compound. Methylaminoacetonitrile was dissolved in dry acetone, and a small amount of sodium methoxide was added, an exothermic reaction taking place with the formation of *5-imino-2 : 2 : 3-trimethyloxazolidine* (X) (cf. the behaviour of aminoacetonitrile, Part III, *loc. cit.*). However, this could not be hydrolysed easily, and under vigorous conditions the *N*-methylglycine amide formed was also decomposed, so that this approach to the amide was unsatisfactory. When *N*-methyl-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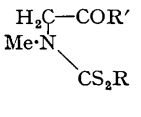
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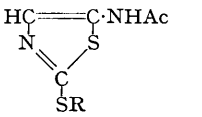
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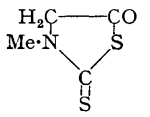
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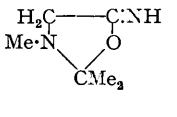
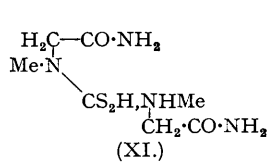

(X.)

glycine amide (prepared by another route) was treated with carbon disulphide, N-*methyl*-N-*carbamylmethylammonium* N-*methyl*-N-*carbamylmethyldithiocarbamate* (XI) was formed which on acidification was rapidly converted into *2-thio-3-methylthiazolid-5-one* (IX). A more convenient preparation consisted in treating carbon disulphide with methylaminoacetonitrile and, without isolating the aminothiazolone which was formed, pouring the mixture into acid, whereupon hydrolysis of the amino-group took place and the desired product slowly separated. On being boiled with water 2-thio-3-methylthiazolid-5-one was hydrolysed to sarcosine and carbon disulphide, and it reacted with 2 equivalents of morpholine to form the *morpholinium* salt (XII) from which it could be recovered by treatment with acid. It dissolved rapidly in sodium hydroxide solution and was recovered on acidification, behaviour which may be compared with that of (III) which cannot be recovered in this way.

An attempt was made to repeat the published preparation of 1-methyl-2 : 4-dithiohydantoin (II; R = Me) mentioned above. Under the conditions outlined in the patent, only tar was obtained but, when the aminothiazoline (IV; R = H) was prepared in methanol and two equivalents of alkali were added, removal of the solvent after 24 hours at 0° gave a water-soluble gum yielding, on acidification, a substance, m. p. 83°, which at first appeared to be the desired product. Instead of being a dithiohydantoin, however, it was identical with 2-thio-3-methylthiazolid-5-one (IX) (a possibility not precluded by the published information which included analysis only for sulphur). This behaviour is fundamentally different from that of the unsubstituted aminothiazole (I) which is split with alkali between the 1- and 2-positions, subsequent ring closure yielding the dithiohydantoin (II; R = H). It must be supposed that 5-amino-2-thio-3-methylthiazolid-5-one is split between the 1- and 5-positions with the formation of a stable alkali salt (VII; R = K, R′ = NH_2) which on acidification is converted into the thiazolidone (cf. XI). This is supported by the reaction of (VII; R = K, R′ = NH_2) with methyl iodide to give *methyl* N-*methyl*-N-*carbamylmethyldithiocarbamate* (VII; R = Me, R′ = NH_2); this was also obtained by the action of methyl iodide on (XI) and was rapidly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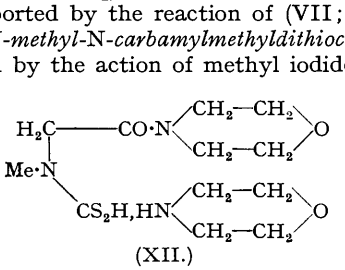
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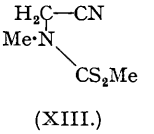
(XIII.)

hydrolysed on being heated with acid or alkali to give (VII; R = Me, R′ = OH). A further indication of the course of this reaction was obtained when the aminothiazoline (IV; R = H) was treated with one equivalent of alkali. Again, a water-soluble salt was obtained, but on acidification 2-thio-3-methylthiazolid-5-one was formed only slowly, and with methyl iodide a different methyl derivative was obtained. The new methyl derivative may be formulated as N-*dithiocarbomethoxy*-N-*methylaminoacetonitrile* (XIII); this was converted by hydrogen iodide into *5-amino-2-methylthio-3-methylthiazolium iodide* (V; R = H), also obtained by the action of methyl iodide on (IV; R = H).

When *iso*propylaminoacetonitrile was mixed with carbon disulphide in solution, no noticeable reaction occurred, but addition of acetic anhydride after 24 hours gave a product

which must, by analogy, be formulated as 5-*acetamido*-2-*thio*-3-iso*propylthiazoline*. It was hydrolysed by acid with the liberation of carbon disulphide, and on being shaken with methyl iodide in alkaline solution afforded 5-*acetamido*-2-*methylthio*-3-iso*propylthiazolium hydroxide*. This was converted into the *iodide* by treatment with hydrogen iodide, and both compounds were converted by hot acid into N-*dithiocarbomethoxy*-N-iso*propylglycine*. When *iso*propylaminoacetonitrile and carbon disulphide were mixed in the presence of benzaldehyde, the *benzylidene* derivative of the aminothiazolidine was formed. Preparation of the aminothiazolidone in solution, followed by hydrolysis with cold mineral acid, gave 2-*thio*-3-iso*propylthiazolid*-5-*one*. This was hydrolysed slowly in boiling water to N-*iso*propylglycine and carbon disulphide, and, on dissolving it in sodium hydroxide and adding methyl iodide, *N*-dithiocarbomethoxy-*N*-*iso*propylglycine was formed. On heating a mixture of *iso*propylaminoacetonitrile and carbon disulphide in solution, a yellow *compound* slowly separated; this had a composition corresponding to $C_{10}H_{13-15}N_3S_4$ but its structure was not established. It was soluble in aqueous sodium hydroxide, from which it was recovered on acidification, and it was converted by hot acetic anhydride into the acetamidothiazolidone.

The difference in the rates of reaction of methyl- and *iso*propyl-aminoacetonitrile seemed to be sufficiently great to be worthy of further investigation and accordingly various other amino-nitriles were allowed to react with carbon disulphide. The qualitative results given below show that the groups attached to both the nitrogen atom and the α-carbon atom influence the reaction rate and that the two effects are roughly additive.

Nitrile.	Reaction rate.
Aminoacetonitrile	++++
Methylaminoacetonitrile	++++
α-Amino-*n*-valeronitrile	+++
α-Methylamino-*n*-valeronitrile	++
α-Methylamino*iso*valeronitrile	+
α-*iso*Propylaminoacetonitrile	+
α-*iso*Propylamino-*n*-valeronitrile	−
α-*iso*Propylamino*iso*valeronitrile	−

The products of these reactions were isolated as their acetyl derivatives, and their constitution as aminothiazoles was established by the formation of carbon disulphide on acid hydrolysis. From α-amino- and α-methylamino-*n*-valeronitrile, compounds formulated as 5-*acetamido*-2-*mercapto*-4-n-*propylthiazole* and 5-*acetamido*-2-*thio*-3-*methyl*-4-n-*propylthiazoline*, respectively, were obtained. In the case of α-methylamino*iso*valeronitrile, acetylation after 5 hours at 20° yielded 5-*acetamido*-2-*thio*-3-*methyl*-4-iso*propylthiazoline*, but after 16 hours an isomeride was obtained which was considered to be 3-*acetyl*-1-*methyl*-5-iso*propyl*-2 : 4-*dithiohydantoin*. Only starting materials could be isolated from the reactions involving the α-*iso*propylaminovaleronitriles.

Experimental.

Reactions with Methylaminoacetonitrile.—Methylaminoacetonitrile (10 g.) in ether (30 c.c.) was added under nitrogen with cooling and stirring to carbon disulphide (10·5 g., 1 equiv.) in ether (20 c.c.). A yellow gum separated which did not crystallise on prolonged scratching. On attempted crystallisation from a variety of solvents, it rapidly darkened. The reaction was repeated in the same volume of ethyl acetate; the product remained in solution and on addition of acetic anhydride (12 g.) 5-*acetamido*-2-*thio*-3-*methylthiazoline* rapidly separated (20 g., 74%). This was recrystallised from ethanol as pale yellow cubes, m. p. 221° (Found: C, 38·6; H, 4·5; N, 14·8. $C_6H_8ON_2S_2$ requires C, 38·3; H, 4·3; N, 14·9%). It dissolved readily in 2N-sodium hydroxide from which it was recovered unchanged after being heated under reflux for 1 hour. When heated with 2N-hydrochloric acid, it slowly passed into solution with the formation of carbon disulphide.

Methylaminoacetonitrile (5 g.) in ethyl acetate (5 c.c.) was added with cooling to a mixture of carbon disulphide (6 g.) and benzaldehyde (8 g.) in ethyl acetate (20 c.c.). On scratching it the *benzylidene* derivative of the aminothiothiazoline separated (12 g., 70%). It crystallised from ethanol as yellow needles, m. p. 187° (Found: C, 56·7; H, 4·7; N, 12·3. $C_{11}H_{10}N_2S_2$ requires C, 56·4; H, 4·3; N, 12·0%).

5-Acetamido-2-thio-3-methylthiazoline (10 g.) was suspended in methanol (30 c.c.) and heated under reflux with methyl iodide (15 g.) for 1 hour, slowly passing into solution and being replaced by 5-*acetamido*-2-*methylthio*-3-*methylthiazolium iodide* (14 g., 80%). This recrystallised from methanol as yellowish-brown cubes, m. p. 212° (Found: C, 25·7; H, 3·4; N, 8·2. $C_7H_{11}ON_2S_2I$ requires C, 25·4; H, 3·4; N, 8·5%). When the iodide (10 g.) was heated under reflux with 2N-hydrochloric acid (50 c.c.) for 1 hour, a clear solution was obtained from which N-*dithiocarbomethoxy*-N-*methylglycine* (4·7 g., 86%) crystallised on cooling. After recrystallisation from water as pale yellow plates, it had m. p. 148° (Found: C, 33·9; H, 5·0; N, 7·8. $C_5H_9O_2NS_2$ requires C, 33·6; H, 5·0; N, 7·8%). This product was also obtained by shaking a solution of sarcosine (1 g.) in 2N-sodium hydroxide (12 c.c.) with carbon disulphide (3 c.c.) for 8 hours; methyl iodide (2 c.c.) was then added and after being shaken for a further hour the aqueous

layer was separated and acidified. The product (1·5 g.) had m. p. **144°**, undepressed on admixture with the ester above.

5-Acetamido-2-mercaptothiazole (this Series, Part III, *loc. cit.*) (5 g.) was suspended in methanol (20 c.c.) and heated under reflux with methyl iodide (8 g.) for 1 hour. The *hydriodide* of 5-acetamido-2-methylthiothiazole (7 g., 78%) crystallised as fawn-coloured needles, m. p. 207—209° (decomp.) (Found: N, 8·6. $C_6H_9ON_2S_2I$ requires N, 8·9%). It dissolved readily in 2N-sodium hydroxide and, on acidification with acetic acid, *5-acetamido-2-methylthiothiazole* was formed, which crystallised from ethanol–water as pale brown needles, m. p. 145° (Found: C, 38·3; H, 4·4; N, 15·1. $C_6H_8ON_2S_2$ requires C, 38·3; H, 4·3; N, 14·9%). When heated under reflux with methyl iodide in methanol, this was converted into the methiodide of 5-acetamido-2-methylthiothiazole, identical with that described above.

Methylaminoacetonitrile (20 g.) was mixed with dry acetone (30 c.c.), and a small amount of sodium methoxide added. An exothermic reaction commenced after which the solution was heated under reflux for 30 minutes. Evaporation *in vacuo* gave a yellow oil which slowly crystallised. This was *5-imino-2 : 2 : 3-trimethyloxazolidine* and crystallised from *iso*propyl ether as pale yellow cubes, m. p. 73° (Found: C, 55·9; H, 9·2; N, 22·2. $C_6H_{10}ON_2$ requires C, 56·2; H, 9·4; N, 21·9%). When this product (10 g.) was dissolved in water (20 c.c.) and heated on a steam-bath, acetone was slowly formed and later ammonia was evolved. Evaporation after 2 hours gave an oil (8 g.) which solidified after distillation at 100°/10^{-5} mm. and was a mixture of *N*-methylglycine amide and unchanged oxazolidine. Pure *N*-methylglycine amide (5 g.) was treated with carbon disulphide (2·5 g.) in methanol (15 c.c.); on cooling and scratching, *N-methyl-N-carbamylmethylammonium N-methyl-N-carbamylmethyldithiocarbamate* separated as pale yellow prisms, m. p. 134° (6·5 g., 90%) (Found: C, 33·7; H, 6·3; N, 21·9. $C_7H_{16}O_2N_4S_2$ requires C, 33·3; H, 6·3; N, 22·2%). When the dithiocarbamate (5 g.) was dissolved in water (25 c.c.) at 0° and acidified with concentrated hydrochloric acid (10 c.c.), *2-thio-3-methylthiazolid-5-one* (2·1 g., 72%) rapidly separated as pale yellow plates. The product had m. p. 78° which was not elevated by recrystallisation from several solvents but a portion sublimed in a high vacuum had m. p. 84° (Found: N, 9·6. $C_4H_5ONS_2$ requires N, 9·5%).

Methylaminoacetonitrile (10 g.) in methanol (10 c.c.) was added, with cooling and stirring under nitrogen, to carbon disulphide (10·5 g.) in methanol (10 c.c.). After 30 minutes, the mixture was poured into ice-cold 4N-hydrochloric acid (150 c.c.) and shaken vigorously for 5 minutes. It was then filtered and after 3 hours at 0° the product was collected, washed with water, and dried *in vacuo* (yield, 13 g., 63%). The product (10 g.) was heated under reflux with water (50 c.c.) for 1 hour, slowly dissolving with the formation of carbon disulphide. Evaporation *in vacuo* gave a gum which crystallised from ethanol as colourless prisms, m. p. 209—211° (3·5 g., 60%). The product did not depress the m. p. of an authentic specimen of sarcosine on admixture.

2-Thio-3-methylthiazolid-5-one (2 g.) in acetone (10 c.c.) was treated with morpholine (2·4 g., 2 equivs.). The mixture became warm and the *morpholinium* salt (XII) of *N*-dithiocarboxy-*N*-methylaminoacetomorpholide (4 g., 90%) separated as pale yellow prisms, m. p. 175—180° (decomp.) (Found: N, 12·9. $C_{12}H_{23}O_3N_3S_2$ requires N, 13·1%). This was readily soluble in water and on acidification the thiazolidone was reformed. 2-Thio-3-methylthiazolid-5-one (1 g.) was shaken with N-sodium hydroxide (14 c.c., 2 equivs.) in which it rapidly dissolved. After 15 minutes, the solution was acidified and the thiazolidone (0·8 g.) recovered.

Methylaminoacetonitrile (10 g.) in methanol (10 c.c.) was added under nitrogen with cooling and stirring to carbon disulphide (10·5 g.) in methanol (20 c.c.). After 30 minutes, potassium hydroxide (16 g.) in methanol (50 c.c.) was added. The solution, which became dark brown, was set aside at 0° for 24 hours and evaporated *in vacuo*. The gum which remained was dissolved in water (200 c.c.) and divided into two equal portions. To the first was added concentrated hydrochloric acid (20 c.c.), a pale brown solid rapidly separating. This was filtered off and washed with water; it proved to be 2-thio-3-methylthiazolid-5-one (8 g., 78%) and did not depress the m. p. of an authentic specimen. The other portion of aqueous solution was shaken with methyl iodide (20 g.), a brown solid being formed. It crystallised from methanol as colourless needles, m. p. 152°, and proved to be *methyl N-methyl-N-carbamylmethyldithiocarbamate* (10 g., 78%) (Found: C, 33·6; H, 5·4; N, 15·4. $C_5H_{10}ON_2S_2$ requires C, 33·6; H, 5·6; N, 15·7%). The same product was formed when *N*-methyl-*N*-carbamylmethylammonium *N*-methyl-*N*-carbamylmethyldithiocarbamate (1 g.) was dissolved in water (5 c.c.) and shaken with methyl iodide (1 g.) (yield, 0·6 g.).

Methylaminoacetonitrile (10 g.) in methanol (10 c.c.) was added in portions to carbon disulphide (10·5 g.) in methanol (20 c.c.) cooled in ice and in an atmosphere of nitrogen. After 30 minutes, potassium hydroxide (8 g.) was added and, after a further hour the solution was evaporated *in vacuo*. The gum was dissolved in water (200 c.c.) and divided into two equal portions. The first was shaken with 4N-hydrochloric acid (60 c.c.) cooled in ice; the solid which first separated dissolved to be replaced by 2-thio-3-methylthiazolid-5-one (7 g., 67%). The second portion was shaken with methyl iodide (20 g.); a brown oil separated which slowly solidified. It crystallised from methanol as pale brown plates, m. p. 74°, and was *N-dithiocarbomethoxy-N-methylaminoacetonitrile* (yield, 8·5 g., 73%) (Found: C, 37·8; H, 5·3; N, 17·7. $C_5H_8N_2S_2$ requires C, 37·5; H, 5·0; N, 17·5%). This product (1 g.) was shaken with 2N-hydriodic acid (10 c.c.) for 1 hour; it slowly dissolved to be replaced by *5-amino-2-methylthio-3-methylthiazolium iodide* (1·5 g.) which crystallised from ethanol as pale yellow needles, m. p. 150° (Found: C, 21·2; H, 3·3; N, 9·6. $C_5H_9N_2S_2I$ requires C, 20·9; H, 3·1; N, 9·7%). Methylaminoacetonitrile (5 g.) in ethyl acetate (5 c.c.) was added with shaking and cooling to carbon disulphide (5·3 g.) in ethyl acetate (10 c.c.). After 30 minutes, methyl iodide (12 g.) was added and the mixture shaken vigorously as an oil separated. The oil rapidly solidified and the product (10 g., 70%) was identical with that last described.

Reactions with iso*Propylaminoacetonitrile.*—Carbon disulphide (8 g.) and *iso*propylaminoacetonitrile (10 g.) were mixed in ethyl acetate (30 c.c.) and set aside at 20° for 16 hours; acetic anhydride (10 g.) was added; *5-acetamido-2-thio-3-isopropylthiazoline* (11 g., 50%) slowly crystallised. It recrystallised from ethyl acetate as yellowish-brown needles, m. p. 163° (Found: C, 44·7; H, 5·5; N, 12·9. $C_8H_{12}ON_2S_2$ requires C, 44·4; H, 5·6; N, 13·0%). The yield was improved to 68% if the initial reaction

mixture contained acetone (10 g.); it is likely that the aminothiazolone was stabilised as its acetone Schiff's base which was later decomposed by the acetic anhydride. The acetamidothiazoline was soluble in sodium hydroxide from which it was recovered on acidification, and with boiling hydrochloric acid evolved carbon disulphide.

*iso*Propylaminoacetonitrile (5 g.) in ethyl acetate (25 c.c.) was mixed with carbon disulphide (4 g.) and benzaldehyde (7 g.). After 20 hours, the *benzylidene* derivative of the aminothiothiazoline was collected (9 g., 68%) and recrystallised from ethanol as yellow plates, m. p. 116° (Found : C, 59·6; H, 5·5; N, 10·7. $C_{13}H_{14}N_2S_2$ requires C, 59·5; H, 5·3; N, 10·7%).

5-Acetamido-2-thio-3-*iso*propylthiazoline (10 g.) was dissolved in 2N-sodium hydroxide (23 c.c.) and shaken with methyl iodide (7 g.). After 1 hour, 5-*acetamido*-2-*methylthio*-3-iso*propylthiazolium hydroxide* (10 g., 86%) was collected and recrystallised from ethyl acetate as pale yellow needles, m. p. 83° (Found : C, 43·3; H, 6·3; N, 10·9. $C_9H_{16}O_2N_2S_2$ requires C, 43·5; H, 6·5; N, 11·3%). When shaken with 2N-hydriodic acid, this was converted into the corresponding *iodide* which crystallised from ethanol–ethyl acetate as yellow prisms, m. p. 182—183° (Found : C, 30·1; H, 4·2; N, 7·5. $C_9H_{15}ON_2S_2I$ requires C, 30·2; H, 4·2; N, 7·8%). When the hydroxide (10 g.) was heated under reflux with 2N-hydrochloric acid (50 c.c.) for 1 hour, an oil formed which solidified on cooling (7 g., 81%). It crystallised from water as colourless plates, m. p. 161°, and was N-*dithiocarbomethoxy*-N-iso*propylglycine* (Found : C, 40·9; H, 6·3; N, 6·8. $C_7H_{13}O_2NS_2$ requires C, 40·6; H, 6·3; N, 6·8%).

A mixture of *iso*propylaminoacetonitrile (10 g.) and carbon disulphide (7·5 g.) in acetone (20 c.c.) was set aside at 20° for 16 hours and then shaken with ice-cold 4N-hydrochloric acid (120 c.c.). The product was filtered after 10 minutes and set aside at 0°; 2-*thio*-3-iso*propylthiazolid*-5-*one* slowly crystallised out. This was collected, washed with water, and dried *in vacuo* (yield, 12 g., 67%). A portion after sublimation in a high vacuum had m. p. 104° (Found : C, 41·2; H, 5·3; N, 7·7. $C_6H_9ONS_2$ requires C, 41·1; H, 5·1; N, 8·0%). The thiazolone (2 g.) dissolved when shaken with N-sodium hydroxide (25 c.c.); methyl iodide (2 g.) was added and, on further shaking, *N*-dithiocarbomethoxy-*N*-*iso*propylglycine (2 g.) was formed; this did not depress the m. p. of the product obtained above.

*iso*Propylaminoacetonitrile (10 g.) and carbon disulphide (15 g.) in ethyl acetate (30 c.c.) were heated under reflux for 3 hours in an atmosphere of nitrogen. The pale yellow *compound* which separated was filtered (yield, 4 g.) and recrystallised unchanged by dissolution in concentrated aqueous ammonia, followed by partial evaporation, as pale yellow prisms, m. p. 223° (Found : C, 39·6; H, 4·6; N, 13·7. $C_{10}H_{13}N_3S_4$ requires C, 39·6; H, 4·3; N, 13·9. $C_{10}H_{15}N_3S_4$ requires C, 39·4; H, 4·9; 13·8%). After this product (2 g.) had been heated with acetic anhydride (10 c.c.) at 100° for 30 minutes, cooling and scratching it yielded 5-acetamido-2-thio-3-*iso*propylthiazolid-5-one (0·8 g.).

Observations on Relative Reactivity of Several Amino-nitriles. The procedure used in each case was to add carbon disulphide (2 g.) in ethyl acetate (2 c.c.) to the amino-nitrile (1 equiv.) in ethyl acetate (2 c.c.) at 20°. The results were as follows :

Aminoacetonitrile : vigorous ebullition.

Methylaminoacetonitrile : vigorous ebullition.

α-Amino-*n*-valeronitrile : mild ebullition. Addition of acetic anhydride (2 g.) after 30 minutes caused the formation of 5-*acetamido*-2-*mercapto*-4-n-*propylthiazole* (2·2 g.) which crystallised from ethanol–ethyl acetate as pale yellow prisms, m. p. 208° (Found : C, 44·5; H, 5·6; N, 12·8. $C_8H_{12}ON_2S_2$ requires C, 44·4; H, 5·6; N, 13·0%).

α-Methylamino-*n*-valeronitrile : solution became warm. Addition of acetic anhydride (2 g.) after 30 minutes gave 5-*acetamido*-2-*thio*-3-*methyl*-4-n-*propylthiazoline* (3 g.). This was recrystallised from ethanol as yellow leaflets, m. p. 211° (Found : C, 47·2; H, 6·3; N, 12·2. $C_9H_{14}ON_2S_2$ requires C, 47·0; H, 6·1; N, 12·2%).

α-Methylamino*iso*valeronitrile : no heat of reaction detected. Addition of acetic anhydride (2 g.) after 5 hours caused the slow crystallisation of 5-*acetamido*-2-*thio*-3-*methyl*-4-iso*propylthiazoline* (2 g.). This was recrystallised from ethanol as pale yellow cubes, m. p. 168° (Found : C, 47·3; H, 6·1; N, 12·0). When addition of the acetic anhydride was delayed for 16 hours, the product was 3-*acetyl*-1-*methyl*-5-iso*propyl*-2 : 4-*dithiohydantoin* (1·8 g.) which recrystallised from glacial acetic acid as colourless cubes, m. p. 213° (Found : C, 47·3; H, 6·3; N, 11·9. $C_9H_{14}ON_2S_2$ requires C, 47·0; H, 6·1; N, 12·2%).

*iso*Propylaminoacetonitrile : no heat of reaction detected.

α-*iso*Propylamino-*n*-valeronitrile : unchanged starting materials recovered after 2 weeks.

α-*iso*Propylamino*iso*valeronitrile : no change after 2 weeks.

Grateful acknowledgment is made of the award of an Australian National University Scholarship (to S. F. C.). We also thank Sir Ian Heilbron, D.S.O., F.R.S., for his interest and encouragement.

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[*Received, May 7th,* 1949.]