Some 2-Nitrothiazoles

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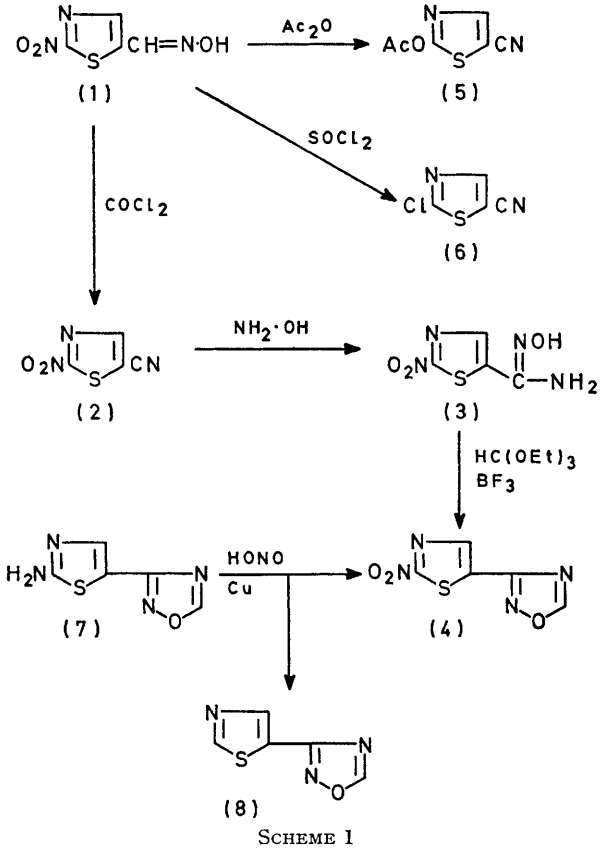
2-Nitrothiazole-5-carbaldehyde oxime (1) is dehydrated by trifluoroacetic anhydride or by phosgene and propene oxide to give the nitrile (2), which has been converted into 3-(2-nitrothiazol-5-yl)-1,2,4-oxadiazole (4). The oxime (1) is converted by acetic anhydride into 2-acetoxythiazole-5-carbonitrile (5) and by thionyl chloride into 2-chlorothiazole-5-carbonitrile (6). 3-(2-Aminothiazol-5-yl)-1,2,4-oxadiazole (7) reacts with nitrous acid in the presence of copper to give the nitro-compound (4), together with the deaminated compound 3-(thiazol-5-yl)-1,2,4-oxadiazole (8). Some similar deaminations have been observed.

SEVERAL 5-nitro-2-furyl-1,2,4-oxadiazoles and oxadiazolines,[1] some analogous 2-furylvinyl-1,2,4-oxadiazoles,[2] and some derivatives of 2-nitrothiazole-5-carbaldehyde [3] have been reported to have antibacterial activity. We decided to study the antibacterial properties of some 2-nitrothiazol-5-yl-1,2,4-oxadiazoles. Only eighteen 2-nitrothiazoles have been described;[3-6] they have all been prepared from diazotized 2-aminothiazoles by the action of nitrous acid (the so-called [7] nitro-Sandmeyer reaction).



SCHEME 1

We prepared 3-(2-nitrothiazol-5-yl)-1,2,4-oxadiazole (4) as shown in Scheme 1. Our first attempt to prepare the nitrile (2), by heating 2-nitrothiazole-5-carbaldehyde in formic acid containing hydroxylamine hydrochloride and sodium formate,[8] gave, as the only identifiable product, 2-chlorothiazole-5-carbonitrile (6). The same chloro-compound (6) was obtained in 55% yield by heating 2-nitrothiazole-5-carbaldehyde oxime (1) with thionyl chloride [9] in ether. Hot acetic anhydride converted the oxime (1) into 2-acetoxythiazole-5-carbonitrile (5).

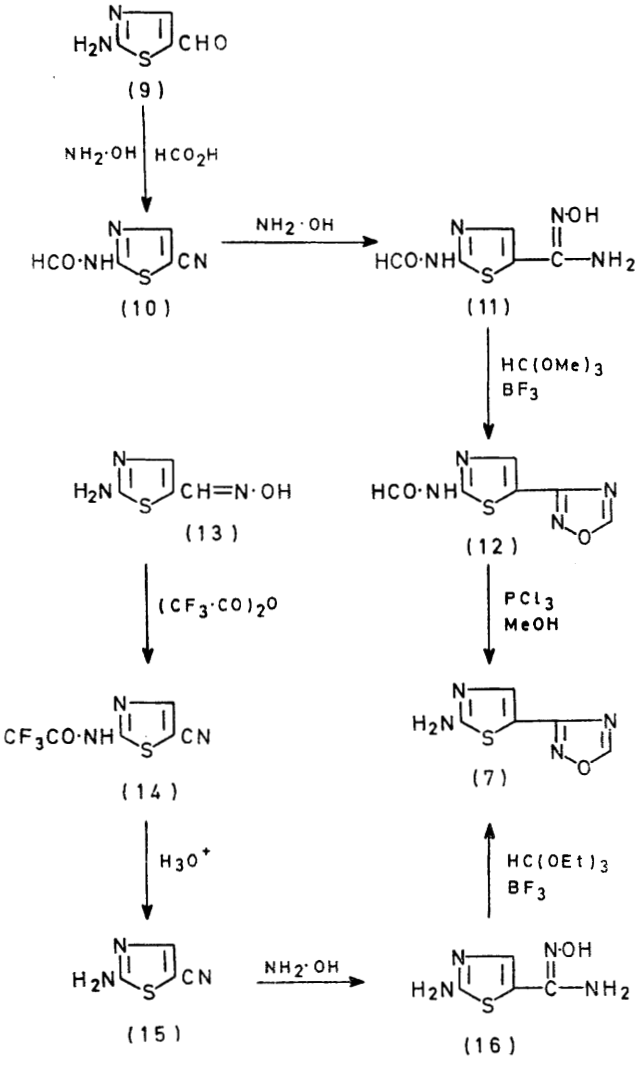
Phenyl isocyanate [10] and trifluoroacetic anhydride both reacted with the oxime (1) to give some of the impure nitrile (2), but the dehydration was finally carried out in better (53%) yield by phosgene and propene oxide in cold ethyl acetate. Dehydration of (1) by phosgene and triethylamine gave the nitrile (2), contaminated by *ca.* 7% of the chloro-compound (6). We have not found any reference to the previous use of phosgene or trifluoroacetic anhydride for the dehydration of oximes.

The chloro-compound (6) was converted into 3-(2-chlorothiazol-5-yl)-1,2,4-oxadiazole through 2-chlorothiazole-5-carboxamide oxime. There is no previous report of the nucleophilic displacement of the nitro-group of a 2-nitrothiazole to give an identified compound. Electron-withdrawing substituents in the 5-position evidently facilitate replacement of the 2-nitro-group, as do those in the 4-position.[6]

The yield of pure 2-nitrothiazole-5-carbaldehyde obtained from the corresponding amine in the nitro-Sandmeyer reaction never exceeded 30%. However 3-(2-aminothiazol-5-yl)-1,2,4-oxadiazole (7), prepared as shown in Scheme 2, when treated with sodium nitrite in fluoroboric acid containing copper powder, was converted into the nitro-compound (4) in 41·5% yield. Some 3-(thiazol-5-yl)-1,2,4-oxadiazole (8) (isolated pure in 6% yield) was always formed in the reaction; it was identical with the oxadiazole prepared from thiazole-5-carbonitrile.[11] 3-(2-Aminothiazol-5-yl)-5-methyl-1,2,4-oxadiazole, prepared similarly to (7), gave the expected nitro-compound in 25% yield, together with a smaller amount of the deaminated thiazole. 2-Aminothiazole-5-carbonitrile (15) underwent the nitro-Sandmeyer reaction, but

[1] Abbott Laboratories, B.P. 1,025,439 (*Chem. Abs.*, 1966, **64**, 19,631).
[2] J. Saikawa and A. Takai, *Yakugaku Zasshi*, 1965, **85**, 948 (*Chem. Abs.*, 1966, **64**, 5073).
[3] G. Asato, G. Berkelhammer, and E. L. Moon, *J. Medicin. Chem.*, 1969, **12**, 374.
[4] B. Prijs, J. Osteitag, and H. Erlenmeyer, *Helv. Chim. Acta*, 1947, **30**, 1200, 2100.
[5] R. A. Parent, *J. Org. Chem.*, 1962, **27**, 2282.
[6] R. J. A. Walsh and K. R. H. Wooldridge, *Chimie thérapeutique*, 1973, 199.
[7] Houben-Weyl, 'Methoden der organischen Chemie,' 4th edn., vol. X/1, G. Thieme, Stuttgart, 1971, p. 836.
[8] T. van Es, *J. Chem. Soc.*, 1965, 2853.
[9] F. P. Doyle, W. Ferrier, D. O. Holland, M. D. Mehta, and J. H. C. Naylor, *J. Chem. Soc.*, 1956, 2853.
[10] T. Mukaikama and H. Nohira, *J. Org. Chem.*, 1961, **26**, 782.
[11] H. Erlenmeyer and R. Morbet, *Helv. Chim. Acta*, 1946, **29**, 1946.

in <20% yield; the major product (up to 30%) was thiazole-5-carbonitrile. Only two amines (4-amino-2-nitrotoluene and *p*-toluidine) have been reported [12] to undergo partial deamination during the nitro-Sandmeyer



SCHEME 2

reaction. Our results are probably not due to the introduction and subsequent removal of a 2-nitro-group, for none of the deaminated product (8) was formed when the nitro-compound (7) was stirred in fluoroboric acid, even after addition of copper powder, and finally of sodium nitrite. It follows that diazonium salts derived from 2-aminothiazoles are unusually susceptible to reduction under the conditions of the nitro-Sandmeyer reaction, possibly by copper or by a lower oxide of nitrogen.

2-Nitrothiazole-5-carbaldehyde reacted with 1,2,4-oxadiazol-3-ylmethyltriphenylphosphonium chloride [13] to give 3-[*trans*-2-(2-nitrothiazol-5-yl)vinyl]-1,2,4-oxadiazole; the corresponding 5-methyl compound was prepared similarly. These oxadiazoles both display powerful antibacterial properties, as do the related compounds (4) and 5-methyl-3-(2-nitrothiazol-5-yl)-1,2,4-oxadiazole.

[12] H. H. Hodgson, F. Heyworth, and E. R. Ward, *J. Chem. Soc.*, 1948, 1512; see also H. H. Hodgson and E. R. Ward, *ibid.*, p. 559.

EXPERIMENTAL

U.v. spectra were measured for solutions in ethanol. T.l.c. was carried out on Merck Kieselgel F_{254} plates in benzene containing various proportions of ethyl acetate. ^{1}H N.m.r. spectra were recorded at 60 MHz.

2-Nitrothiazole-5-carbonitrile (2).—2-Nitrothiazole-5-carbaldehyde oxime [3] (2·00 g) in dry ethyl acetate (152 ml) was stirred at 0° and propene oxide (1·64 g) was added. A solution of phosgene (2·28 g) in benzene (25 ml) was added at 2—4° during 20 min. The solution was warmed to 22° during 14 min, then left at 20—22° for 1 h. It was washed with 1% (w/v) sodium hydrogen carbonate solution (2 × 25 ml) then thrice with water, dried (Na_2SO_4), and evaporated. Steam-distillation of the residue and extraction of the distillate (800 ml) with chloroform gave the nitrile (1·14 g, 60·5%), m.p. 77—82°, of 88% purity (g.l.c.). A *sample* pressed on a porous plate had m.p. 79—82°, $\lambda_{max.}$ 250 and 303 nm (ε 7900 and 10,000) (Found: C, 31·4; H, 0·8; N, 26·8. $C_4HN_3O_2S$ requires C, 31·1; H, 0·65; N, 27·1%). The same product was obtained in 32% yield by slowly adding the oxime to 1·05 equiv. of trifluoroacetic anhydride in ethyl acetate at 0°.

2-Chlorothiazole-5-carbonitrile (6).—2-Nitrothiazole-5-carbaldehyde oxime (1·00 g) was suspended in dry diethyl ether (10 ml). Thionyl chloride (3 ml) was added to the stirred suspension, and 20 min later more thionyl chloride (3 ml) was added. Refluxing was maintained during the addition and for 10 min thereafter. The solvent and most of the thionyl chloride were removed under reduced pressure, and the dark, residual oil was dissolved in ethanol and treated with charcoal. Filtration and removal of the ethanol left the nitrile as a yellow solid (455 mg, 55%). A sample sublimed *in vacuo* was >99% pure; it had m.p. 54—55°, $\lambda_{max.}$ 241 and 256 nm (ε 6300 and 8800). This compound sublimes too readily to be analysed accurately. The same product (i.r. spectrum) was obtained in 5·5% yield (after steam-distillation) by heating the oxime (1) with hydroxylamine hydrochloride and sodium formate [7] in formic acid.

2-Acetoxythiazole-5-carbonitrile (5).—The oxime (1) (680 mg) was dissolved in warm acetic anhydride (15 ml) and fused sodium acetate (100 mg) was added. The mixture was heated on a water-bath for 15 min, then the acetic anhydride was removed under reduced pressure. The residue was extracted with boiling light petroleum (b.p. 40—60°), giving the *acetoxy-compound* (300 mg, 45%), m.p. 69—71°, $\lambda_{max.}$ 265 nm (ε 7800) (Found: C, 42·6; H, 2·5; N, 16·7; S, 18·2. $C_6H_4N_2O_2S$ requires C, 42·6; H, 2·5; N, 16·7; S, 19·0%).

2-Nitrothiazole-5-carboxamide Oxime (3).—2-Nitrothiazole-5-carbonitrile (3·474 g) was added in portions, during 10 min, with stirring, at 4—9°, to the hydroxylamine solution (final vol. 270 ml) prepared from hydroxylamine hydrochloride (4·76 g) and sodium ethoxide. The orange solution was left for 30 min, then the solvent was removed below 50°. The residue was dissolved in ethyl acetate (250 ml) and extracted into 2N-hydrochloric acid (total 200 ml). The acid extract was filtered and neutralized (solid $NaHCO_3$). Isolation with ethyl acetate gave the amide oxime (2·74 g, 69%), m.p. 160° (decomp.). Recrystallization of a sample from water gave clusters of red *needles*, m.p. 172° (decomp.),

[13] J. A. Claisse, M. W. Foxton, G. I. Gregory, A. H. Sheppard, E. P. Tiley, W. K. Warburton, and M. J. Wilson, *J.C.S. Perkin I*, 1973, 2241.

$\lambda_{max.}$ 248, 303, and 371 nm (ε 6950, 4300, and 3000) (Found: C, 25·8; H, 2·3; N, 29·6. $C_4H_4N_4O_3S$ requires C, 25·5; H, 2·1; N, 29·8%).

3-(2-*Nitrothiazol-5-yl*)-1,2,4-*oxadiazole* (4).—The preceding compound (4·00 g) was dissolved in warm triethyl orthoformate (24 ml) containing boron trifluoride–ether complex (5 drops). The solution was boiled for 13 min. Evaporation under reduced pressure left a brown residue, which was dissolved in ethanol and shaken with charcoal. Filtration and evaporation left the crude oxadiazole (4·035 g, 96%). Recrystallization from methanol (8·3 ml) gave the *oxadiazole* (2·04 g, 48·5%), m.p. 77—78°, $\lambda_{max.}$ 221 and 318·5 nm (ε 5800 and 3600) (Found: C, 30·5; H, 1·2; N, 28·6; S, 16·1%; M^+, 197·9845. $C_5H_2N_4O_3S$ requires C, 30·3; H, 1·0; N, 28·2; S, 16·2%; *M*, 197·9848).

2-*Chlorothiazole-5-carboxamide Oxime*.—2-Chlorothiazole-5-carbonitrile (717 mg) was dissolved in the hydroxylamine solution prepared in methanol (20 ml) from hydroxylamine hydrochloride (700 mg) and sodium methoxide. After 40 min the solution was evaporated to dryness. The residue was recrystallized from benzene to give the *amide oxime* (376 mg, 43%), m.p. 148—149° (decomp.), $\lambda_{max.}$ 253 and 295 nm (ε 5400 and 4900) (Found: C, 27·6; H, 2·4; N, 23·7; S, 18·1. $C_4H_4ClN_3OS$ requires C, 27·0; H, 2·3; N, 23·6; S, 18·0%).

3-(2-*Chlorothiazol-5-yl*)-1,2,4-*oxadiazole*.—The preceding compound (8·50 g) was dissolved in triethyl orthoformate (57 ml) containing boron trifluoride–ether complex (20 drops) and the solution was boiled for 20 min. Removal of the solvent under reduced pressure, steam-distillation of the residue, and extraction of the distillate (1·7 l) with chloroform gave the *oxadiazole* (6·02 g, 73·5%), m.p. 76·5—77·5°, $\lambda_{max.}$ 265 nm (ε 11,400) (Found: C, 31·95; H, 1·1; Cl, 18·45; N, 22·8; S, 16·8%; M^+, 186·9618. $C_5H_2ClN_3OS$ requires C, 31·9; H, 1·1; Cl, 18·9; N, 22·4; S, 17·05%; *M*, 186·9608).

2-*Formamidothiazole-5-carbonitrile* (10).—2-Aminothiazole-5-carbaldehyde [14] (101 g), sodium formate (123 g), and hydroxylamine hydrochloride (66·7 g) were heated under reflux in formic acid (1·025 l) for 1 h. Most of the formic acid was removed under reduced pressure, then water (1·5 l) was added, and finally saturated sodium hydrogen carbonate solution (6 l). The solid was filtered off, washed with water, and dissolved in ethanol (4 l), and the solution was shaken with charcoal. Filtration and removal of the solvent left the *nitrile* (51·45 g, 37%), m.p. 227—229°, $\lambda_{max.}$ 284 nm (ε 12,500) (Found: C, 39·1; H, 2·1; N, 27·7; S, 20·8. $C_5H_3N_3O_3S$ requires C, 39·2; H, 2·0; N, 27·45; S, 20·95%).

2-*Formamidothiazole-5-carboxamide Oxime* (11).—The preceding compound (51·0 g) when treated with hydroxylamine in methanol as described for (3), gave the amide oxime (47·7 g, 76·5%), m.p. 185° (decomp.). A *sample* recrystallized from water had m.p. 193° (decomp.), $\lambda_{max.}$ 295·5 nm (ε 9600) (Found: C, 31·7; H, 3·4; N, 30·3; S, 17·65. $C_5H_6N_4O_2S$ requires C, 32·3; H, 3·25; N, 30·1; S, 17·2%).

3-(2-*Formamidothiazol-5-yl*)-1,2,4-*oxadiazole* (12).—Boron trifluoride–ether complex (100 drops) was added to stirred, redistilled trimethyl orthoformate (300 ml). The preceding compound (19·1 g) was added to the stirred solution, which was then warmed on a steam-bath, with stirring. The solid dissolved during 15 min. Heating was continued for 20 min more, then the warm mixture was filtered. The residue was washed with ethyl acetate. The combined filtrates were evaporated below 40°, and the orange residue was dissolved in ethyl acetate (3 l). The solution was washed with 0·5N-hydrochloric acid (5 × 800 ml), then with saturated sodium hydrogen carbonate solution (2 × 400 ml), and finally with water, dried ($MgSO_4$), and evaporated under reduced pressure. The residue in methanol was treated with charcoal, giving the oxadiazole (13·6 g, 67·5%), m.p. *ca.* 200° (decomp.). A *sample* recrystallized from methanol had m.p. 198°, $\lambda_{max.}$ 291 nm (ε 14,800) (Found: C, 36·7; H, 2·1; N, 28·7; S, 16·0. $C_6H_4N_4O_2S$ requires C, 36·7; H, 2·1; N, 28·6; S, 16·3%).

3-(2-*Aminothiazol-5-yl*)-1,2,4-*oxadiazole* (7).—The preceding compound (23·1 g) was dissolved in warm methanol, and the solution was cooled to −4°. Phosphorus trichloride (31·65 ml) was added dropwise, under strictly anhydrous conditions, during 12 min, to the stirred solution. The temperature rose to 6°. The mixture was stirred for 45 min at room temperature, then saturated sodium hydrogen carbonate solution (1·17 l) was added, and finally water (500 ml). Isolation with ethyl acetate gave the amine (7·73 g, 92%). A *sample* recrystallized from methanol (charcoal) had m.p. 157—158°, $\lambda_{max.}$ 299·5 nm (ε 16,300) (Found: C, 35·5; H, 2·3; N, 33·4; S, 19·1. $C_5H_4N_4OS$ requires C, 35·7; H, 2·4; N, 33·3; S, 19·0%).

3-(2-*Nitrothiazol-5-yl*)-1,2,4-*oxadiazole* (4) *by the Nitro-Sandmeyer Reaction*.—Copper powder (precipitated; 7·15 g) was added to a solution of sodium nitrite (71·4 g) in water (final vol. 357 ml), and the mixture was cooled to 3°. 3-(2-Aminothiazol-5-yl)-1,2,4-oxadiazole (12·0 g) was dissolved in aqueous 20% (w/v) fluoroboric acid (135 ml) and the solution was added in one portion, during <30 s, to the vigorously stirred and externally cooled solution of sodium nitrite at such a rate that the addition was complete before frothing interfered with the mixing of the liquids. The temperature rose to 12°. Stirring was continued without cooling for 1·5 h. The mixture was filtered and the residue was washed with ethyl acetate (2 × 300 ml). The filtrate was extracted with the ethyl acetate washings, then with more ethyl acetate (4 × 300 ml). The ethyl acetate solution was warmed with charcoal, filtered, dried ($MgSO_4$), and evaporated, leaving the crude nitro-compound (9·185 g, 65·5%). The nitro-compound from several experiments (18·43 g) was chromatographed in benzene–ethyl acetate (95 : 5 v/v) on silica gel MFC (1·5 kg). After removal of a trace of fast-running material, the nitro-compound was eluted in 5·8 l. Evaporation left analytically pure 3-(2-nitrothiazol-5-yl)-1,2,4-oxadiazole (11·87 g, 41%), m.p. 76—77·5°, identical (i.r., n.m.r., and g.l.c.) with the compound already described. In a separate experiment, further elution of the column gave 3-(thiazol-5-yl)-1,2,4-oxadiazole (6%), m.p. 83—86°, identical (i.r. spectrum) with the compound described later.

3-(2-*Acetamidothiazol-5-yl*)-5-*methyl*-1,2,4-*oxadiazole*.— A suspension of 2-formamidothiazole-5-carboxamide oxime (4·0 g) in acetic anhydride (200 ml) was boiled for 2·5 h. The acetic anhydride was removed under reduced pressure and the residue was stirred with saturated sodium hydrogen carbonate solution. Isolation with ethyl acetate (charcoal) gave a yellow solid (4·84 g, 75%), m.p. 278°. Recrystallization from methanol–tetrahydrofuran gave the *oxadiazole*, m.p. 281°, $\lambda_{max.}$ 291 nm (ε 16,300) (Found: C, 43·0; H, 3·7; N, 24·5; S, 13·8. $C_8H_8N_4O_2S$ requires C, 42·9; H, 3·6; N, 24·9; S, 14·3%).

3-(2-*Aminothiazol-5-yl*)-5-*methyl*-1,2,4-*oxadiazole*.— Deacetylation of the previous compound was carried out as described for the deformylation of (11). The amine, m.p. 240° (decomp.), was obtained in 97% yield; a *sample* recrystallized from ethyl acetate had m.p. 240° (decomp.),

$\lambda_{max.}$ 298·5 nm (ε 15,700) (Found: C, 39·45; H, 3·4; N, 30·8; S, 17·1. $C_6H_6N_4OS$ requires C, 39·6; H, 3·3; N, 30·7; S, 17·6%).

5-Methyl-3-(2-nitrothiazol-5-yl)-1,2,4-oxadiazole.— Treatment of the preceding compound with nitrous acid and copper, as described for the amine (7), gave the crude oxadiazole (19) in 71% yield. It was purified similarly to (4), giving the *nitro-compound* (19) (25%), m.p. 119—120°, $\lambda_{max.}$ 320 nm (ε 9700), τ ($CDCl_3$) 7·29 (Me) and 1·55 (thiazole 4-H) (Found: C, 34·25; H, 2·0; N, 25·8; S, 15·2. $C_6H_6N_4O_3$ requires C, 33·95; H, 1·9; N, 26·4; S, 15·1%). Further elution of the column gave 5-methyl-3-(thiazol-5-yl)-1,2,4-oxadiazole (20%), m.p. 87—88°, raised to 93—95° by vacuum sublimation, $\lambda_{max.}$ 257 nm (ε 9500), τ ($CDCl_3$) 7·35 (Me), 1·45 (thiazole 4-H), and 1·05 (thiazole 2-H) (Found: C, 43·7; H, 3·2; N, 24·9. $C_6H_5N_3OS$ requires C, 43·1; H, 3·0; N, 25·15%).

2-Aminothiazole-5-carbaldehyde Oxime (13).—2-Aminothiazole-5-carbaldehyde [14] (0·5 g), hydroxylamine hydrochloride (0·5 g), pyridine (0·5 ml), and ethanol (5 ml) were heated together under reflux for 1·5 h, then the solution was evaporated to dryness. The residue was washed with water to give the *oxime* (0·45 g, 80%), m.p. 208—209°, $\lambda_{max.}$ 244 and 299·5 nm (ε 2200 and 17,100) (Found: C, 34·0; H, 3·6; N, 28·6. $C_4H_5N_3OS$ requires C, 33·5; H, 3·5; N, 29·3%).

2-Trifluoroacetamidothiazole-5-carbonitrile (14).—The preceding compound (6·37 g) was suspended in dry ethyl acetate (170 ml). Trifluoroacetic anhydride (15·8 ml) was added dropwise, with stirring, during 1 h, between −2 and −5°. After 1 h more, the solvent was removed under reduced pressure. The residue in benzene was filtered; removal of the benzene left the nitrile (9·0 g, 90%), m.p. 180—184°, raised to 184—186° by crystallization from benzene, $\lambda_{max.}$ 287 nm (ε 11,400) (Found: C, 32·9; H, 1·1; F, 24·55; N, 19·1; S, 14·8. $C_6H_2F_3N_3OS$ requires C, 32·6; H, 0·95; F, 25·8; N, 19·0; S, 14·55%).

2-Aminothiazole-5-carbonitrile (15).—The preceding compound (11·7 g) was stirred for 1 h with aqueous 20% (w/v) fluoroboric acid (120 ml) at 73—75°. The solution was cooled, shaken with charcoal, filtered, and neutralized (solid $NaHCO_3$). Extraction with ethyl acetate (2 × 500 ml), concentration, and cooling gave the *amine* (6·16 g, 95·5%), m.p. 208—211°, raised to 212—213° by crystallization from water, $\lambda_{max.}$ 290·5 nm (ε 13,600) (Found: C, 38·1; H, 2·6; N, 33·1. $C_4H_3N_3S$ requires C, 38·4; H, 2·4; N, 33·6%).

2-Aminothiazole-5-carboxamide Oxime (16).—Treatment of the preceding compound with hydroxylamine in methanol at 5° for 48 h, as described for (3), gave the amide oxime, m.p. 145° (decomp.) (69·5%). A *sample* recrystallized from methanol had m.p. 147° (decomp.), $\lambda_{max.}$ 292·5 nm (ε 11,100) (Found: C, 29·7; H, 3·8; N, 34·4; S, 19·5. $C_4H_6N_4OS$ requires C, 30·4; H, 3·8; N, 35·4; S, 20·3%).

Reaction of 2-Aminothiazole-5-carboxamide Oxime with Triethyl Orthoformate.—The preceding compound (5·04 g) was heated in triethyl orthoformate (30 ml) containing boron trifluoride–ether complex (4 drops) at 80° for 1·25 h. The reaction was worked up as described for (12), giving the oxadiazole (2·34 g, 43%), identical (i.r. spectrum) with the compound (7) already described.

Thiazole-5-carboxamide Oxime (with Dr. H. Fazakerley). —Thiazole-5-carbonitrile [11] (8·35 g) in ethanol (25 ml) was added to the hydroxylamine solution prepared from hydroxylamine hydrochloride (7·9 g) and anhydrous sodium carbonate (6·0 g) in water (20 ml) and ethanol (20 ml). After 20 h the solution was concentrated and water (70 ml) was added, giving the *amide oxime* (9·06 g, 83%), m.p. 156—159°, raised to 159—160° by recrystallization from water, $\lambda_{max.}$ 284 nm (ε 4100) (Found: C, 33·8; H, 3·5; N, 29·6; S, 22·3. $C_4H_5N_3OS$ requires C, 33·6; H, 3·5; N, 29·4; S, 22·4%).

3-(Thiazol-5-yl)-1,2,4-oxadiazole (8) (with Dr. H. Fazakerley).—The preceding compound (1·45 g) was boiled for 1·25 h with triethyl orthoformate (5 ml) containing boron trifluoride–ether complex (1 drop). Removal of the solvent and recrystallization of the residue from aqueous ethanol gave the *oxadiazole* (0·94 g, 61%), m.p. 89—90°, $\lambda_{max.}$ 255 nm (ε 9900) (Found: C, 39·1; H, 2·1; N, 27·5; S, 20·5. $C_5H_3N_3OS$ requires C, 39·2; H, 2·0; N, 27·4; S, 20·9%).

3-Chloromethyl-5-methyl-1,2,4-oxadiazole.—A mixture of chloroacetamide oxime (6·4 g) and acetic anhydride (12·2 g) was stirred at 130° for 2 h. The mixture was left at room temperature overnight, neutralized with sodium hydrogen carbonate, and extracted with ethyl acetate. The extract was washed with water, dried (Na_2SO_4), and evaporated. Distillation of the residue gave the oxadiazole (4·53 g, 58%), b.p. 84—89° at 17 mmHg, $\nu_{max.}$ (Nujol) 756 and 770 cm^{-1} (C–Cl), τ ($CDCl_3$) 5·42 (CH_2) and 7·40 (CH_3).

(5-Methyl-1,2,4-oxadiazol-3-ylmethyl)triphenylphosphonium Chloride.—A solution of the preceding compound (4·0 g) and triphenylphosphine (9·0 g) in acetonitrile (75 ml) was boiled for 18 h. Removal of the solvent and washing with benzene gave the *phosphonium chloride* (9·1 g, 76%), m.p. 206°, $\lambda_{max.}$ 226·5 nm (ε 26,900) (Found: C, 66·9; H, 5·1; Cl, 8·9; N, 6·8. $C_{22}H_{20}ClN_2OP$ requires C, 67·0; H, 5·1; Cl, 9·0; N, 7·1%).

3-[trans-2-(2-Nitrothiazol-5-yl)vinyl]-1,2,4-oxadiazole.— (1,2,4-Oxadiazol-3-ylmethyl)triphenylphosphonium chloride [13] (3·81 g) was suspended in dimethyl sulphoxide (25 ml). 1,5-Diazabicyclo[4.3.0]non-5-ene (1·57 g) was added, with stirring, and after 10 min 2-nitrothiazole-5-carbaldehyde (1·50 g) was added. The mixture was stirred for 2 h, then poured into water. Isolation with ethyl acetate and chromatography on silica in benzene containing up to 10% ethyl acetate gave the *vinyl compound* (1·3 g, 58%), m.p. 165—166° (from methanol), $\lambda_{max.}$ 261 and 358 nm (ε 9500 and 13,700) (Found: C, 37·6; H, 1·9; N, 25·3; S, 14·3. $C_7H_4N_4O_3S$ requires C, 37·5; H, 1·8; N, 25·0; S, 14·3%).

5-Methyl-3-[trans-2-(2-nitrothiazol-5-yl)vinyl]-1,2,4-oxadiazole.—This *compound* was prepared and purified similarly to the preceding compound, in 34% yield; it had m.p. 158—160·5°, $\lambda_{max.}$ 260 and 361 nm (ε 10,900 and 15,400) (Found: C, 40·6; H, 2·6; N, 23·8; S, 13·1. $C_8H_6N_4O_3S$ requires C, 40·35; H, 2·5; N, 23·6; S, 13·5%).

[14] A. Dorlans, Ger.P. 1,182,234 (*Chem. Abs.*, 1965, **62**, 7764).

[3/1160 *Received, 5th June*, 1973]