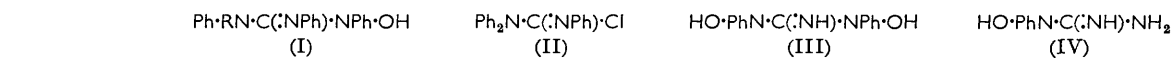
1143. *Some Reactions of* 3-*Amino*-5,5-*dimethyl*-2-*phenyl*-1,2,4-*oxadiazoline.*

By R. Hull and R. Farrand.

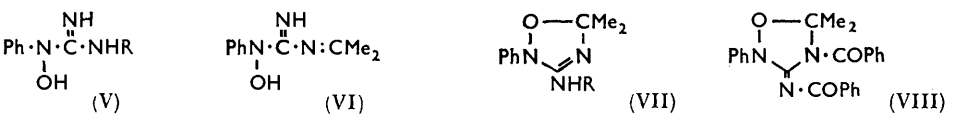
The product obtained from phenylhydroxylamine, cyanamide, and acetone is shown to be 3-amino-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline. This compound has been used as an intermediate in the synthesis of *N*-hydroxy-*N*-phenylguanidines, *N*-hydroxy-*N*-phenylaminopyrimidines, oxadiazolopyrimidines, and other compounds.

A few *N*-hydroxy-*N*-phenylguanidines have been described. Busch and his co-workers [1] obtained the hydroxytriphenylguanidine (I; R = H) by reaction of diphenylcarbodiimide with an equimolecular proportion of phenylhydroxylamine, Ley and Winkler [2] prepared the hydroxytetraphenylguanidine (I; R = Ph) from the chloro-amidine (II) and phenylhydroxylamine, and Wieland [3] made the dihydroxydiphenylguanidine (III) from



cyanogen bromide and phenylhydroxylamine. However, no synthesis has yet been reported of the hydroxy-phenylguanidine (V) and it is only recently that the parent hydroxyguanidine (IV), prepared from cyanamide and hydroxylamine, has been obtained pure.[4]

We found that cyanamide reacted readily with phenylhydroxylamine in acetone solution. The product, however, was not the expected *N*-hydroxy-*N*-phenylguanidine (V; R = H), but a substance, $C_{10}H_{13}N_3O$, which did not reduce Fehling's solution or give the hydroxylamine test with tetrazolium salt.[5] It was therefore either the oxadiazoline (VII; R = H) or, less probably, the isopropylidene derivative (VI). It formed a mono-



acetyl derivative and, with adipoyl chloride in pyridine, a diamide, $C_{26}H_{32}N_6O_4$. The infrared absorption spectrum of its dibenzoyl derivative, $C_{24}H_{21}N_3O_3$, showed amidic carbonyl peaks only at 1655 (mull) and 1695 cm.$^{-1}$ (chloroform solution) and appeared to be most consistent with structure (VIII). It appears therefore that the compound $C_{10}H_{13}N_3O$ has structure (VII; R = H).

In this paper we describe investigations carried out using the oxadiazoline (VII; R = H) as an intermediate in the synthesis of a wide variety of novel compounds for use as potential chemotherapeutic agents.

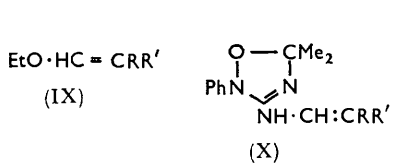
Sulphonamides.—The oxadiazoline (VII; R = H) was condensed with *m*-nitrobenzenesulphonyl chloride and *p*-acetamidobenzenesulphonyl chloride in acetone–pyridine to give the corresponding sulphonamides which, on short treatment with hot dilute hydrochloric acid, gave the hydroxy-guanidines (V; R = $SO_2{\cdot}C_6H_4{\cdot}NO_2$-*m*) and (V; R = $SO_2{\cdot}C_6H_4{\cdot}NH_2$-*p*), respectively.

Reactions with Acrylic Acid Derivatives.—The reaction of certain amino-compounds

[1] Busch, Blume, and Pungs, *J. prakt. Chem.*, 1909, 2, **79**, 513.
[2] Ley and Winkler, *Ber.*, 1914, **47**, 2945.
[3] Wieland, *Ber.*, 1904, **37**, 1536.
[4] Kalyankar, Ikawa, and Snell, *J. Biol. Chem.*, 1958, **233**, 1175.
[5] Snow, *J.*, 1954, 2588.

with ethyl β-ethoxy-α-ethoxycarbonylacrylate (IX; R = R′ = CO_2Et) has provided a useful synthetic route to a wide variety of heterocyclic compounds (see, *e.g.*, ref. 6).

Reaction at room temperature during 2 days of ethyl β-ethoxy-α-ethoxycarbonylacrylate with the oxadiazoline (VII) gave the oxadiazolylaminomethylenemalonate (X; R = R′ = CO_2Et) which ring-closed under heat treatment to the oxadiazolopyrimidine (XI; R = CO_2Et, X = O). The infrared absorption spectrum gave, as a mull, only one carbonyl peak at 1695 cm.$^{-1}$; however, resolution was effected in chloroform solution into the ester-carbonyl (1752 cm.$^{-1}$) and ring-carbonyl (1700 cm.$^{-1}$). An attempt to hydrolyse

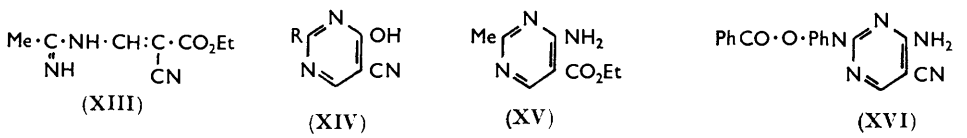


(IX) (X) (XI) (XII)

the oxadiazolopyrimidine into the *N*-hydroxy-*N*-phenylpyrimidine (XII; R = OH, R′ = CO_2H) was unsuccessful; instead it was converted into 5-carboxyuracil.

A similar reaction was then carried out with ethyl α-cyano-β-ethoxyacrylate (IX; R = CN, R′ = CO_2Et) and the amino-oxadiazoline (VII) in methylene dichloride, which furnished the acrylonitrile (X; R = CN, R′ = CO_2Et). Ethanol was eliminated on attempted purification and gave the cyanopyrimidine (XI; R = CN, X = O). With difunctional groups (CN and CO_2Et) in the side-chain of the oxadiazoline (X; R = CN, R′ = CO_2Et) two alternative modes of cyclisation are possible to give either the cyanopyrimidine (XI; R = CN, X = O) or the ethoxycarbonylpyrimidine (XI; R = CO_2Et, X = NH).

The acetamidinoacrylate (XIII) has been shown [7] to ring-close under the effect of alkali to the cyanopyrimidine (XIV; R = Me) and under neutral or acid conditions to the ethoxycarbonylpyrimidine (XV). In the presence of sodium ethoxide in alcohol, the ester (X; R = CN, R′ = CO_2Et) cyclises to a cyanopyrimidine but scission of the oxazol-



(XIII) (XIV) (XV) (XVI)

dine ring takes place at the same time to yield, as a final product, 5-cyanouracil (XIV; R = OH). Cyclisation of the ester (X; R = CN, R′ = CO_2Et) in alcoholic hydrochloric acid gives the 2-(*N*-hydroxy-*N*-phenylamino)pyrimidine (XII; R = NH_2, R′ = CO_2Et). Although two hydroxyaminopyrimidines have been described [8] *N*-hydroxy-*N*-phenylaminopyrimidines appear to be new.

The reaction of the oxadiazoline (VII) with α-cyano-β-ethoxyacrylonitrile (IX; R = R′ = CN) has also been investigated. Refluxing the two compounds in methylene dichloride solution gave a compound, $C_{14}H_{13}N_5O$. It was not possible to distinguish between the two possible structures (X; R = R′ = CN) and (XI; R = CN, X = NH). Elimination of acetone occurred when the compound was heated in alcoholic solution and the *N*-hydroxy-*N*-phenylaminopyrimidine (XII; R = NH_2, R′ = CN) was isolated. The same pyrimidine was obtained when the oxadiazoline (VII) and α-cyano-β-ethoxyacrylonitrile were heated together in alcoholic solution. That a free hydroxyl group was present

[6] Williams, *J.*, 1962, 2222, and preceding papers.
[7] Todd and Bergel, *J.*, 1937, 364; Foldi and Salamon, *Ber.*, 1941, **74**, 1126.
[8] Pfleiderer and Ferch, *Annalen*, 1958, **615**, 52; Sirakawa, *J. Pharm. Soc. Japan*, 1959, **79**, 1477.

in this pyrimidine was proved by the formation of an *O*-benzoyl derivative (XVI) whose infrared absorption spectra gave an ester carbonyl at 1780 cm.$^{-1}$.

Miscellaneous Reactions.—An attempt to prepare the hydrazino-compound (VII; R = NH_2) by reaction of the oxadiazoline (VII) with hydrazine in acetic acid solution (cf. ref. 9) failed; instead, we obtained a compound, $(C_3H_7N_2O)_n$, whose infrared absorption spectrum showed bands at 3390 (NH), *ca.* 2700—2800 (NH_2^+), and 1695 cm.$^{-1}$ ($C{=}N^+$). The proton magnetic resonance spectrum showed a doublet associated with the methyl groups of an isopropylidene group, τ 8·00 and 8·05, and a singlet associated with a methyl of an acetate group, τ 7·92. There were no aromatic protons. The above data corresponded with the acetate of isopropylideneaminoguanidine, $Me_2C{:}N{\cdot}NH{\cdot}C(:NH){\cdot}NH_2$. The picrate of our material was identical with that of isopropylideneaminoguanidine.[10]

Fusion of the oxadiazoline (VII) with tristrichloromethyl-1,3,5-triazine gave the 3-(bistrichloromethyltriazinyl) derivative.

Experimental

Phenylhydroxylamine.—It was not found necessary to distil the nitrobenzene or to estimate the strength of the zinc dust (cf. Vogel, "A Text Book of Practical Organic Chemistry," Longmans, London, 1948, p. 629). The following is a typical preparation. Zinc dust (260 g.) was added during 15 min. to a vigorously stirred mixture of nitrobenzene (168 ml.), ammonium chloride (100 g.), and water (3·2 l.). The temperature rose to 65—70°. The hot mixture was filtered and the residue washed with hot water (400 ml.). Sodium chloride (1·2 kg.) was added with stirring to the filtrates which were cooled and placed in an ice-bath for 1 hour. The solid was collected and extracted with ether (3 × 250 ml.), the extract was washed with water, dried ($MgSO_4$), and the solvent removed to yield phenylhydroxylamine (110—120 g.), m. p. 78—80° (lit., 81°), which was used without further purification. It could be stored in a refrigerator for a few days.

3-Amino-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline (VII; R = H).—Cyanamide (28·9 ml., 50% aqueous solution) was added to a cooled solution of phenylhydroxylamine (60 g.) in acetone (130 ml.) and the mixture was kept for 2 hr. at 30—40°, and then heated to reflux for 30 min. The following morning, excess of reagent was removed under reduced pressure. The residue was dissolved in ether (350 ml.), the extract was washed with water and dried (Na_2SO_4), and the ether was removed. Recrystallisation of the residue from cyclohexane (carbon) gave the *product* (21·5 g.), m. p. 111—113°, as prismatic needles; a further recrystallisation raised the m. p. to 122—123° (Found: C, 62·8; H, 6·9; N, 22·2. $C_{10}H_{13}N_3O$ requires C, 62·8; H, 6·8; N, 22·0%). The compound did not reduce Fehling's solution.

3-Acetamido-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline (VII; R = Ac).—Acetyl chloride (0·5 ml.) was added dropwise to a cooled solution of 3-amino-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline (0·5 g.) in pyridine (1 ml.). After 1 hr. the mixture was added to ice–water, to yield an oil which solidified on standing (m. p. 86—92°), to give the *acetyl derivative*, needles, m. p. 94—96° (from cyclohexane) (Found: C, 61·1; H, 6·2; N, 17·6. $C_{12}H_{15}N_3O_2$ requires C, 61·7; H, 6·4; N, 18·0%).

NN'-di-(5,5-dimethyl-2-phenyl-1,2,4-oxadiazolin-3-yl)adipamide.—Adipoyl chloride (1·8 g.) was added dropwise to an ice-cooled solution of 3-amino-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline (4 g.) in pyridine (50 ml.). After 1 hr. the mixture was added to ice–water. The solid was collected; recrystallisation from aqueous alcohol gave the *adipamide* (2·2 g.) as plates, m. p. 172°. A further recrystallisation raised the m. p. to 178—179° (Found: C, 63·3; H, 6·4; N, 16·8. $C_{26}H_{32}N_6O_4$ requires C, 63·4; H, 6·5; N, 17·1%).

4-Benzoyl-3-benzoylimino-2-phenyl-1,2,4-oxadiazolidine (VIII).—Benzoyl chloride (1 ml.) in pyridine (1 ml.) was added slowly to a solution of 3-amino-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline (0·6 g.) in pyridine (2 ml.) below 10°. The following morning, the mixture was added to ice–water. The resultant solid was washed with 5N-sodium hydrogen carbonate and water, and dried, to give the *dibenzoyl derivative*, prismatic needles, m. p. 155—156° (from cyclohexane) (Found: C, 72·0; H, 5·1; N, 11·1. $C_{24}H_{21}N_3O_3$ requires C, 72·2; H, 5·25; N, 10·5%), $\nu_{max.}$ (mull) 1655, ($CHCl_3$ solution) 1695 cm.$^{-1}$ (both amidic CO).

[9] Stolle and Krauch, *Ber.*, 1913, **46**, 2337; G.P. 673,588; G.P. 962,165; B.P. 495,514; B.P. 891,553.
[10] Finnegan, Henry, and Smith, *J. Amer. Chem. Soc.*, 1952, **74**, 2981.

5,5-*Dimethyl*-3-(m-*nitrobenzenesulphonamido*)-2-*phenyl*-1,2,4-*oxadiazoline* (VII; R = $SO_2 \cdot C_6H_4 \cdot NO_2$-*m*).—*m*-Nitrobenzenesulphonyl chloride (16·05 g.) was added during 30 min. to a solution of 3-amino-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline (14·15 g.) in acetone (75 ml.) and pyridine (11·2 ml.) at 20—25°. After stirring for 2 hr. the *sulphonamide* (3·8 g.) was collected and washed with acetone; it formed needles, m. p. 140—142° (from alcohol) (Found: C, 51·1; H, 4·2; N, 14·9. $C_{16}H_{16}N_4O_5S$ requires C, 51·1; H, 4·25; N, 14·9%), $\nu_{max.}$ (in KBr) 1380, 1365 cm.$^{-1}$ (Me_2C).

N-*Hydroxy*-N′-*nitrobenzenesulphonyl*-N-*phenylguanidine* (V; R = $SO_2 \cdot C_6H_4NO_2$-*m*).—5,5-Dimethyl-3-(*m*-nitrobenzenesulphonamido)-2-phenyl-1,2,4-oxadiazoline (0·5 g.), in alcohol (5 ml.) and 2N-hydrochloric acid (5 ml.), was heated under reflux for 2 hr. The mixture was filtered from a little insoluble material, and cooled. The *phenylhydroxyguanidine* (0·25 g.) formed needles, m. p. 174—176° (decomp.) (from aqueous alcohol) (Found: C, 46·3; H, 3·7; N, 16·5. $C_{13}H_{12}N_4O_5S$ requires C, 46·5; H, 3·6; N, 16·7%). There was no *gem*-dimethyl infrared absorption. The compound gave a dark green colour with Fehling's solution.

3-(p-*Acetamidobenzenesulphonamido*)-5,5-*dimethyl*-2-*phenyl*-1,2,4-*oxadiazoline*.—*p*-Acetamidobenzenesulphonyl chloride (8·8 g.) was added portionwise to a stirred solution of 3-amino-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline (7·6 g.) in pyridine (6·0 ml.) and acetone (40 ml.) at 20—25° during 30 min. After a further 90 min. the *sulphonamide* (7·3 g.), m. p. 180° (decomp.), was collected and washed with acetone. It formed needles, m. p. 183—184° (decomp.) (from 2-ethoxyethanol) (Found: C, 55·9; H, 5·1; N, 14·4; S, 8·6. $C_{18}H_{20}N_4O_4S$ requires C, 55·6; H, 5·15; N, 14·4; S, 8·25%).

N-p-*Aminobenzenesulphonyl*-N′-*hydroxy*-N′-*phenylguanidine*.—3-(*p*-Acetamidobenzenesulphonamido)-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline (7·25 g.) was heated under reflux in N-hydrochloric acid (75 ml.) for 1½ hr. After cooling, the *hydroxyguanidine hydrochloride* (3·3 g.) was collected, needles, m. p. 196° (decomp.) (from N-hydrochloric acid) (Found: C, 42·5; H, 4·9; Cl^-, 9·5; N, 15·0. $C_{13}H_{14}N_4O_3S,HCl,1\frac{1}{2}H_2O$ requires C, 42·3; H, 4·9; Cl^-, 9·6; N, 15·2%). The compound gave a positive test for a primary arylamine by diazotisation and coupling with sodium 2-hydroxynaphthalene-3,6-disulphonate.

3-(2,2-*Diethoxycarbonylvinylamino*)-5,5-*dimethyl*-2-*phenyl*-1,2,4-*oxadiazoline* X; (R = R′ = CO_2Et).—A mixture of 3-amino-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline (10·3 g.) and ethyl β-ethoxy-α-ethoxycarbonylacrylate (11·63 g.) in ethanol (7·5 ml.) and water (7·5 ml.) was shaken for 2 days. Water (100 ml.) was added and the mixture was extracted with ether (3 × 30 ml.). The extracts were combined and washed successively with water, dilute hydrochloric acid, water, then dried (Na_2SO_4), and concentrated to yield an oil (16 g.) which solidified on standing. Crystallisation from aqueous ethanol (carbon) gave the *vinylamino-oxadiazoline* as needles, m. p. 72—74° (Found: C, 59·8; H, 6·6; N, 11·7. $C_{18}H_{23}N_3O_5$ requires C, 59·8; H, 6·4; N, 11·6%).

Ethyl 1,5-*Dihydro*-3,3-*dimethyl*-5-*oxo*-1-*phenyl*[1,2,4]*oxadiazolo*[4,3-a]*pyrimidine*-6-*carboxylate* (XI; R = CO_2Et, X = O).—(*a*) A mixture of 3-amino-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline (15·3 g.) and ethyl β-ethoxy-α-ethoxycarbonylacrylate (8·6 g.) was heated with stirring on a steam-bath for 1 hr. Recrystallisation of the reaction mixture from aqueous ethanol (carbon) gave the *oxadiazolopyrimidine* (3·9 g.) as prisms, m. p. 86—88° (Found: C, 60·9; H, 5·2; N, 13·6. $C_{16}H_{17}N_3O_4$ requires C, 60·95; H, 5·4; N, 13·3%), $\nu_{max.}$ (mull) 1695 (CO , ($CHCl_3$) 1700 (ring CO), 1752 cm.$^{-1}$ (ester CO).

(*b*) 3-(2,2-diethoxycarbonylvinylamino)-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline (0·5 g.) was heated at 120°(bath) for 2 hr. The product, after trituration with light petroleum, was identical (i.r.) with that obtained in (*a*).

Hydrolysis of the Oxadiazolopyrimidine.—The above oxadiazolopyrimidine (0·5 g.) in 2N-hydrochloric acid (5 ml.) was heated under reflux for 2 hr. The crystals which separated were crystallised from water to yield 5-carboxyuracil,[11] m. p. 281—283° (decomp.) (Found: C, 38·5 H, 2·7; N, 18·2. Calc. for $C_5H_4N_2O_4$: C, 38·5; H, 2·6; N, 18·0%), $\lambda_{max.}$ (in 0·1N-HCl) 274 mμ (ε 10,600), (in 0·1N-NaOH) 293 mμ (ε 13,550).

3-(2-*Cyano*-2-*ethoxycarbonylvinylamino*)-5,5-*dimethyl*-2-*phenyl*-1,2,4-*oxadiazoline* (X; R = CN, R′ = CO_2Et).—3-Amino-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline (0·96 g.) and ethyl α-cyano-β-ethoxyacrylate (0·8 g.) in methylene dichloride (10 ml.) were heated under reflux for 1 hr. The solution was evaporated and the residue was triturated with aqueous ethanol.

[11] Langley, *J. Amer. Chem. Soc.*, 1956, **78**, 2136.

Filtration gave the *cyano-ethoxycarbonylvinylamino-oxadiazoline* as prisms, m. p. 122—124° (Found: C, 61·4; H, 5·7; N, 17·9. $C_{16}H_{18}N_4O_3$ requires C, 61·2; H, 5·7; N, 17·85%), $\nu_{max.}$ (mull) 3280 cm.$^{-1}$ (NH). Ethanol was eliminated from the compound on recrystallisation from ethanol to yield 6-*cyano*-1,5-*dihydro*-3,3-*dimethyl*-5-*oxo*-1-*phenyl*[1,2,4]*oxadiazolo*[4,3-a]*pyrimidine* as prismatic needles, m. p. 197—199° (Found: C, 62·5; H, 4·4; N, 20·9. $C_{14}H_{12}N_4O_2$ requires C, 62·7; H, 4·5; N, 20·9%). There was no NH infrared absorption.

Ethyl 4-*Amino*-2-(N-*hydroxy*-N-*phenylamino*)*pyrimidine*-5-*carboxylate* (XII; R = CN, R′ = CO_2Et).—3-(2-Cyano-2-ethoxycarbonylvinylamino)5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline (0·5 g.) in ethanol (10 ml.) and 10N-hydrochloric acid (0·25 ml.) was heated under reflux for ½ hr. Excess of reagent was removed under diminished pressure. The *pyrimidine hydrochloride* crystallised from ethanol in needles, m. p. 190° (decomp.) (Found: N, 18·2. $C_{13}H_{14}N_4O_3$,HCl requires N, 18·4%). Adjustment of a hot aqueous solution of the hydrochloride to pH 8 with sodium hydrogen carbonate solution gave the *pyrimidine base*, which crystallised as pale mauve needles, m. p. 150—152° (from ethanol) (Found: C, 56·8; H, 5·2; N, 20·3. $C_{13}H_{14}N_4O_3$ requires C, 56·9; H, 5·1; N, 20·45%).

Action of Sodium Ethoxide on 3-(2-*Cyano*-2-*ethoxycarbonylvinylamino*)-5,5-*dimethyl*-2-*phenyl*-1,2,4-*oxadiazoline.*—Alcoholic sodium ethoxide [from sodium (0·12 g.) and ethanol (10 ml.)] was added to a filtered solution of the oxadiazoline (1·6 g.) in alcohol (40 ml.) and the whole was heated under reflux for 5 min. After cooling, the solid (0·5 g.) was collected, dissolved in water, and the filtered solution adjusted to pH 2 with 5N-hydrochloric acid. The solid was washed with water. Recrystallisation from water (carbon) gave 5-cyanouracil as prisms, m. p. (slow decomp.) from 280° (Found: C, 43·6; H, 2·3; N, 30·6. Calc. for $C_5H_3N_3O_2$: C, 43·8; H, 2·2; N, 30·6). The infrared absorption spectrum (mull) was identical with that of 5-cyanouracil prepared by Shaw's [12] method.

Reaction of 3-*Amino*-5,5-*dimethyl*-2-*phenyl*-1,2,4-*oxadiazoline with* α-*Cyano*-β-*ethoxyacrylonitrile.*—The oxadiazoline (9·6 g.) and α-cyano-β-ethoxyacrylonitrile (6·1 g.) in methylene dichloride (200 ml.) were heated under reflux for 1 hr. Excess of reagent was removed under diminished pressure, and trituration of the residual oil with ethanol (100 ml.) gave a product (8·25 g.), needles, m. p. 154—156° (from ethanol) (carbon) (Found: C, 62·8; H, 4·8; N, 26·1. $C_{14}H_{13}N_5O$ requires C, 62·9; H, 4·9; N, 26·2%). It was not possible to decide if the product was 3-(2,2-dicyanovinylamino)-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline or the ring-closed compound.

4-*Amino*-5-*cyano*-2(N-*hydroxy*-N-*phenylamino*)*pyrimidine.*—(*a*) The above product (1·0 g.) in ethanol (15 ml.) was heated under reflux for 90 min., carbon was added, and the whole was filtered. Cooling yielded the *pyrimidine* (0·35 g.), m. p. 184—186° (decomp.) (Found: C, 57·8; H, 3·9; N, 30·5. $C_{11}H_9N_5O$ requires C, 58·1; H, 3·95; N, 30·8%).

(*b*) 3-Amino-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline (9·6 g.) and α-cyano-β-ethoxyacrylonitrile (6·1 g.) in ethanol (100 ml.) were heated under reflux for 1 hr. Cooling yielded the pyrimidine (6·0 g.), m. p. 179—181° (decomp.), identical with the above (infrared). The infrared spectrum showed a typical trace for an amino-pyrimidine.

4-*Amino*-2-(N-*benzoyloxy*-N-*phenylamino*)-5-*cyanopyrimidine* (XVI).—Benzoyl chloride (1·4 ml.) was added to an ice-cooled solution of 4-amino-5-cyano-2-(N-hydroxy-N-phenylamino)-pyrimidine (1·1 g.) in pyridine (10 ml.). After 2½ hr. the mixture was poured into ice–water (50 ml.). The precipitate of the *benzoyloxyamino-pyrimidine* formed micro-needles, m. p. 172—173° (from ethanol) (carbon) (Found: C, 65·2; H, 4·1; N, 21·2. $C_{18}H_{13}N_5O_2$ requires C, 65·2; H, 3·95; N, 21·15%), $\nu_{max.}$ (mull) 1780 cm.$^{-1}$ (ester CO).

Reaction of 3-*Amino*-5,5-*dimethyl*-2-*phenyl*-1,2,4-*oxadiazoline with Hydrazine.*—The oxadiazoline (7·6 g.) and 100% hydrazine hydrate (4 ml.) in acetic acid (4·8 ml.) were heated on a steam-bath for 2 hr.; ammonia was given off. After a few days, crystallisation was induced, and the solid (3·5 g.) washed with acetone, to give needles, m. p. 222—224° (decomp.) (from ethanol) (Found: C, 41·4; H, 8·1; N, 32·5. $(C_3H_7N_2O)_n$ requires C, 41·4; H, 8·1; N, 32·2%). The picrate, prepared in aqueous solution, formed prismatic needes, m. p. 206° (decomp.) (from water) (Found: C, 35·2; H, 4·0; N, 28·6. Calc. for $C_{10}H_{13}N_7O_7$: C, 35·0; H, 3·8; N, 28·6%). The decomposition point was undepressed on admixture with isopropylideneaminoguanidine picrate.[10] The picrates had identical infrared spectra. The above product, $(C_3H_7N_2O)_2$, was therefore *isopropylideneaminoguanidine acetate.*

[12] Shaw, *J.*, 1955, 1834.

3-(4,6-*Bistrichloromethyl*-1,3,5-*triazin*-2-*ylamino*)-5,5-*dimethyl*-2-*phenyl*-1,2,4-*oxadiazoline*.—A mixture of 3-amino-5,5-dimethyl-2-phenyl-1,2,4-oxadiazoline (0·96 g.) and tristrichloromethyl-1,3,5-triazine (2·17 g.) was fused on a water-bath during 1 hour. Extraction of the cooled melt with aqueous ethanol gave the *product* as pale yellow plates, m. p. 153—155° (Found: C, 35·8; H, 2·8; N, 16·6. $C_{15}H_{12}Cl_6N_6O$ requires C, 35·65; H, 2·4; N, 16·65%).

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