Quaternary Salts from 2-Chloro-5-nitropyrimidines. Part I. Preparation and Some Reactions.

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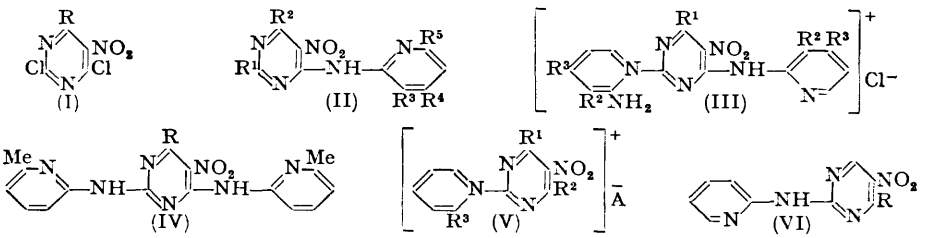
The reaction of several 2 : 4-dichloro- and 2-chloro-5-nitropyrimidines with pyridine, 2-aminopyridine, and 2-amino-3(or 4)-methylpyridine yielded, in general, quaternary salts formed *via* the 2-chloro-substituent of the pyrimidine; the 4-chloro-substituent (when present) condensed normally with the amino-group. When 2-amino-6-methylpyridine reacted with 2 : 4-dichloro-6-methyl- or 2 : 4-dichloro-5-nitropyrimidine no quaternary salt was formed; condensation occurred between the amino-group and, successively, the 4- and the 2-chloro-substituent. Replacement of the aminopyridyl substituent in the 2-position of the pyrimidine quaternary salts by alkoxy- and amino-groups was investigated.

REACTION of 2 : 4-dichloro- or 2 : 4-dichloro-6-methyl-5-nitropyrimidine (I; R = H or Me) with ammonia has led, according to the conditions, to substitution of one chlorine substituent, or of both, to yield 4-amino-2-chloro- or 4-amino-2-chloro-6-methyl-5-nitropyrimidine or the corresponding diaminopyrimidines (Gabriel and Colman, *Ber.*, 1901, **34**, 1244; Gabriel and Isay, *Ber.*, 1906, **39**, 230). Condensation of the dichloropyrimidines with α-amino-esters and -ketones has yielded analogous products (Boon, Ramage, and Jones, *J.*, 1951, 96; Boon and Jones, *ibid.*, p. 591; Polonovski and Jerome, *Compt. rend.*, 1950, **230**, 392). In all cases the 4-chlorine atom in the pyrimidine is the first to be substituted. However, we found that the compound (I; R = H) (1 mol.) and 2-aminopyridine (2 mols.) gave only a small amount of the expected product (II; $R^1 = Cl$, $R^2 = R^3 = R^4 = R^5 = H$) in methanol at 0°, the main product being a yellow crystalline solid soluble in water, containing ionic chlorine, and derived from two mols. of 2-amine and one of the chloro-compound with the loss of one mol. of hydrochloric acid. Since the same compound was also obtained by treating a boiling solution of the base (II; $R^1 = Cl$, $R^2 = R^3 = R^4 = R^5 = H$) in methanol with one mol. of 2-aminopyridine, or by treating the pyrimidine (I; R = H) with three mols. of 2-aminopyridine in hot methanol, it appeared to be the quaternary salt (III; $R^1 = R^2 = R^3 = H$). Strong evidence for this structure and against formulation as the hydrochloride of 5-nitro-2 : 4-di-2′-pyridylaminopyrimidine is derived from the reaction of 2-amino-6-methylpyridine with 2 : 4 dichloro- or 2 : 4-dichloro-6-methyl-5-nitropyrimidine (see below) in hot methanol which



yields respectively the bases (IV; R = H or Me), insoluble in water. Finally the ultraviolet spectra of compounds (III; $R^2 = Me$, $R^1 = R^3 = H$) and (IV; R = H) show a very marked difference which could not exist unless the former was a quaternary salt;

thus the former in 0·05N-hydrochloric acid had maxima at 340 and 229 mμ (ε 9500 and 23,100 respectively) and a minimum 322 mμ (ε 9200), and the latter in 0·1N-hydrochloric acid had maxima at 330·5 and 239·5 (ε 29,800 and 13,800 respectively) and minima at 266·5 and 223·0 mμ (ε 7340 and 11,100 respectively).

Again, in methanol at 0°, the pyrimidine (I; R = Me) and 2-aminopyridine yielded an analogous quaternary salt (III; R^1 = Me, R^2 = R^3 = H).

When 2 : 4-dichloro-5-nitropyrimidine was treated in boiling methanol with 4 mols. of 2-aminopyridine the quaternary salt (III; R^1 = R^2 = R^3 = H) was precipitated initially but on continued boiling passed into solution. On cooling, a new compound, m. p. 148°, was precipitated. Since this was also formed when the quaternary salt was treated in boiling methanol with 2-aminopyridine, and when 2-chloro-5-nitro-4-2′-pyridylaminopyrimidine (II; R^1 = Cl, R^2 = R^3 = R^4 = R^5 = H) was treated with sodium methoxide in methanol, it is 2-methoxy-5-nitro-4-2′-pyridylaminopyrimidine (II; R^1 = MeO, R^2 = R^3 = R^4 = R^5 = H). Similar compounds were formed in boiling methanol from 2 : 4-dichloro-5-nitropyrimidine and the 3- and the 4-methyl homologue of 2-aminopyridine, and from 2 : 4-dichloro-6-methyl-5-nitropyrimidine. Reaction in boiling ethanol gave ethoxypyrimidines.

Confirmation that the 2-chlorine atom in the pyrimidine is involved in the quaternisation has been obtained in two ways. 2-Amino-4-chloro-6-methyl-5-nitropyrimidine, unequivocally synthesised by the action of phosphoryl chloride on 2-amino-4-hydroxy-6-methyl-5-nitropyrimidine (Boon, Ramage, and Jones, *J.*, 1951, 96), with 2-aminopyridine gave a product identical with that obtained by heating the quaternary salt (III; R^1 = Me, R^2 = R^3 = H) with methanolic ammonia. Again the quaternary salt (III; R^1 = R^2 = R^3 = H) with ammonia yielded what must be 2-amino-5-nitro-4-2′-pyridylaminopyrimidine (II; R^1 = NH_2, R^2 = R^3 = R^4 = R^5 = H) since it differs from the product (VI; R = NH_2) obtained from 4-amino-2-chloro-5-nitropyrimidine and 2-aminopyridine. Aniline reacted similarly with (III; R^1 = R^2 = R^3 = H). This evidence also confirms the structure (II; R^1 = Cl, R^2 = R^3 = R^4 = R^5 = H) for the minor product of the reaction of the pyrimidine (I; R = H) with 2-aminopyridine since, as shown earlier, the corresponding 2-methoxy-compound (II; R^1 = MeO, R^2 = R^3 = R^4 = R^5 = H) is obtained by replacement either of the chlorine atom in this compound or of the aminopyridine residue in the salt (III; R^1 = R^2 = R^3 = H) by a methoxy-group. The replacement by amino- or alkoxy-groups of the 2-aminopyridine residue in quaternary salts of the type described above provides a new approach to 2-amino- and 2-alkoxy-pyrimidines which will be further described later.

Returning now to the typical reaction involving formation of a quaternary salt, we sought to examine the effect of various substitutions in the aminopyridine and the pyrimidine component. From the reaction of the pyrimidine (I; R = Me) with 2-amino-3- and 2-amino-4-methylpyridine, only the salts (III; R^1 = R^3 = H, R^2 = Me, and R^1 = R^2 = H, R^3 = Me) were obtained; similarly 2-aminopyridine gave only the salt (III; R^1 = Me, R^2 = R^3 = H). However, neither of the dichloropyrimidines (I; R = H or Me) with 2-amino-6-methylpyridine gave a quaternary salt, one or both of the chlorine atoms being replaced by the methylpyridylamino-residue. The absence of quaternary salt formation may be attributed to a steric effect of methyl and substituted amino-groups which flank the pyridine nitrogen atom. Bergstrom and Siegel (*J. Amer. Chem. Soc.*, 1952, **74**, 254) point out that quaternisation of 2 : 4 : 6-trimethylpyridine by sulphonic acid esters is apparently slower than that of pyridine. Antaki and Petrov (*J.*, 1951, 551) found that ethyl β-aminocrotonate and 2-aminopyridine form 4 : 10-dihydro-2-methyl-4-oxo-1 : 10-diazanaphthalene and the same ring-closure occurs with amino-methylpyridines, with however the exception of 2-amino-6-methylpyridine where steric hindrance appears to prevent reaction. Lappin (*J. Amer. Chem. Soc.*, 1948, **70**, 3348) reported a similar effect when amino-methylpyridines react with ethoxymethylenemalonate. When 6-amino-2 : 4-dichloro-5-nitropyrimidine and 2-aminopyridine reacted at 0° no quaternisation was observed, the product being the base (II; R^2 = NH_2, R^1 = Cl, R^3 = R^4 = R^5 = H). Prolonged reaction at room temperature produced a mixture of this compound and the quaternary salt (III; R^1 = NH_2, R^2 = R^3 = H).

Other quaternary salts have been made from pyridine or 2-aminopyridine and 2-chloropyrimidines in benzene or acetone (see Experimental Section).

Quaternary salts which show some analogy with ours were made by Zincke (*Annalen*, 1904, **330**, 361), Zincke, Heuser, and Möller (*ibid.*, 1904, **333**, 296) (who used pyridine) and Vompe and Turitsyna (*Doklady Akad. Nauk S.S.S.R.*, 1950, **74**, 509; *Chem. Abs.*, 1951, **45**, 3846) (who used 3- and 4-aminopyridine) for reaction with 1-chloro-2 : 4-dinitrobenzene. With 2-aminopyridine, however, only 2-(2 : 4-dinitrophenylamino)pyridine was formed. The fact that no quaternary salt was formed in this case was attributed by Vompe and Turitsyna to a steric hindering effect involving, perhaps, both the pyridine-amino-group and the *o*-nitro-group in the chlorodinitrobenzene. This postulate could be applied to our experiences since this *o*-nitro-group could have a greater *ortho*-effect than the annular nitrogen atom of the 2-chloro-5-nitropyrimidines. We have found that quaternary salt formation occurs only with the 2- and not with the 4-chlorine atom, which could be hindered by the 5-nitro-group. In a preliminary publication (*Chem. and Ind.*, 1951, 937) we mentioned some of the points dealt with in this paper.

Experimental

M. p.s were determined in an electrically heated copper block.

Reaction of 2 : 4-*Dichloro-5-nitropyrimidine with* 2-*Aminopyridine.*—(a) *With* 2 *mols. of* 2-*aminopyridine.* To an ice-cold solution of 2 : 4-dichloro-5-nitropyrimidine (4·2 g.) in methanol (25 ml.) was slowly added an ice-cold solution of 2-aminopyridine (4·1 g.) in methanol (25 ml.). A yellow solid rapidly separated; after 2 hr. at 0° it was collected and washed with methanol. This solid (4·8 g.) was separated by hot water into the insoluble 2-*chloro-5-nitro-4-2′-pyridyl-aminopyrimidine* (0·9 g.), yellow sword-shaped prisms (from ethanol), m. p. 156° (Found: C, 43·3; H, 2·6; N, 27·2. $C_9H_6O_2N_5Cl$ requires C, 43·0; H, 2·4; N, 27·8%), and the 2-*amino*-1-(5-*nitro-4-2′-pyridylamino-2-pyrimidyl*)*pyridinium chloride* (III; $R^1 = R^2 = R^3 = H$) (3·6 g.), yellow prismatic needles (from water or, better, dilute hydrochloric acid), m. p. 249° (decomp.) (Found: C, 49·1; H, 3·5; N, 28·25; Cl^-, 10·4. $C_{14}H_{13}O_2N_7Cl$ requires C, 48·8; H, 3·2; N, 28·4; Cl, 10·3%). The latter affords the *bromide*, needles (from water), m. p. 262° (decomp.) (Found: C, 42·8; H, 3·9; N, 23·95. $C_{14}H_{12}O_2N_7Br$ requires C, 43·2; H, 2·85; N, 25·1%), and *iodide*, orange needles (from water), m. p. 252° (decomp.) (Found: C, 38·5; H, 3·2; N, 21·1. $C_{14}H_{12}O_2N_7I$ requires C, 38·85; H, 2·5; N, 22·4%).

(b) *With* 3 *mols. of* 2-*aminopyridine.* From the reactants in boiling methanol the quaternary chloride separated quantitatively [m. p. 249° (decomp.)].

2-Chloro-5-nitro-4-2′-pyridylaminopyrimidine (0·2 g.) and 2-aminopyridine (0·4 g.) in hot methanol (15 ml.) gave the same chloride immediately, having m. p. 249° (decomp.) (Found: N, 28·0%).

(c) *With* 4 *mols. of* 2-*aminopyridine.* When to a hot solution of 2 : 4-dichloro-5-nitropyrimidine (0·98 g.) in methanol (25 ml.) was added 2-aminopyridine (1·9 g.), the quaternary chloride separated. Continued boiling, however, gave a clear solution which on cooling deposited a pale yellow solid. Crystallisation of this solid from ethanol gave 2-methoxy-5-nitro-4-2′-pyridylaminopyrimidine, m. p. 148° alone or mixed with the compound prepared as below.

2-*Methoxy-5-nitro-4-2′-pyridylaminopyrimidine.*—To a solution of sodium (0·5 g.) in methanol (10 ml.) was added a solution of 2-chloro-5-nitro-4-2′-pyridylaminopyrimidine (0·5 g.) in methanol (15 ml.), and the resulting orange-red solution refluxed for 2 hr. The solution was acidified with dilute acetic acid and cooled and the yellow solid collected and washed with water. Crystallisation from ethanol gave yellow plates of 2-*methoxy-5-nitro-4-2′-pyridylaminopyrimidine*, m. p. 148° (Found: C, 48·5; H, 3·9; N, 28·6. $C_{10}H_9O_3N_5$ requires C, 48·6; H, 3·7; N, 28·3%).

2-*Ethoxy-5-nitro-4-2′-pyridylaminopyrimidine.*—The 2-chloro-compound was boiled with a solution of sodium ethoxide in ethanol for 2 hr. The 2-*ethoxypyrimidine* crystallised from ethanol as pale yellow needles, m. p. 131° (Found: C, 51·0; H, 4·95; N, 27·5. $C_{11}H_{11}O_3N_5$ requires C, 50·6; H, 4·25; N, 26·8%).

This pyrimidine, m. p. and mixed m. p. 131°, was also obtained when the quaternary chloride (III; $R^1 = R^2 = R^3 = H$) was refluxed with 2-aminopyridine in ethanol.

Reaction of 2 : 4-*Dichloro-6-methyl-5-nitropyrimidine and* 2-*Aminopyridine.*—The *salt* (III; $R^1 = Me$, $R^2 = R^3 = H$) was obtained exclusively when the dichloro-compound was treated with 2-aminopyridine in ice cold methanol. It crystallised from water containing a few drops

of dilute hydrochloric acid in yellow needles, m. p. 215° (decomp.) (Found : C, 49·5; H, 4·0; N, 26·75. $C_{15}H_{14}O_2N_7Cl$ requires C, 50·0; H, 3·9; N, 27·2%).

4 Mols. of 2-aminopyridine and 1 mol. of the dichloropyrimidine, when refluxed in methanol, gave 2-*methoxy*-6-*methyl*-5-*nitro*-4-2′-*pyridylaminopyrimidine*, yellow prisms (from ethanol), m. p. 137° (Found : C, 50·7; H, 5·01; N, 26·53. $C_{11}H_{11}O_3N_5$ requires C, 50·6; H, 4·25; N, 26·8%).

Reaction in ethanol gave a deep red solution. This was evaporated to dryness, the residue was exhaustively extracted with hot benzene, and the cooled extract filtered through a column of alumina. The yellow eluate was evaporated to dryness, and the residue crystallised from ethanol, to yield yellow needles of 2-*ethoxy*-6-*methyl*-5-*nitro*-4-2′-*pyridylaminopyrimidine*, m. p. 113—114° (Found : C, 53·2; H, 4·8; N, 26·4. $C_{12}H_{13}O_3N_5$ requires C, 52·4; H, 4·8; N, 25·5%).

4-*Amino*-5-*nitro*-2-2′-*pyridylaminopyrimidine*.—2-Chloro-4-amino-5-nitropyrimidine (0·5 g.) (Isay, *Ber.*, 1906, **39**, 250) and 2-aminopyridine (1 g.) were heated at 120—130° for 1 hr. The melt was then triturated with 50% ethanol and the brown solid collected, dissolved in hot N/20-hydrochloric acid, and reprecipitated with ammonia. 4-*Amino*-5-*nitro*-2-2′-*pyridylaminopyrimidine* crystallised from aqueous pyridine as pale yellow needles, m. p. 276° (Found : N, 36·5. $C_9H_8O_2N_6$ requires N, 36·2%).

2-*Amino*-5-*nitro*-4-2′-*pyridylaminopyrimidine*.—(*a*) 2-Chloro-5-nitro-4-2′-pyridylaminopyrimidine (0·5 g.) was refluxed for 2 hr. with methanolic ammonia (15 ml. of a saturated solution of ammonia in methanol, and 15 ml. of methanol). The bright yellow precipitated 2-*amino-compound* crystallised from butan-1-ol as yellow plates, m. p. 251—252° (Found : C, 46·3; H, 3·9; N, 36·0. $C_9H_8O_2N_6$ requires C, 46·5; H, 3·5; N, 36·2%).

(*b*) A suspension of the quaternary salt (III; $R^1 = R^2 = R^3 = H$) (0·5 g.) in methanol (20 ml.) was treated with concentrated ammonia solution (3 ml.), a deep red solution being obtained. After 2 hours' refluxing the solution had become pale yellow and, on cooling, yellow plates of 2-amino-5-nitro-4-2′-pyridylaminopyrimidine (0·3 g.) separated, having m. p. and mixed m. p. 251—252°.

2-*Anilino*-5-*nitro*-4-2′-*pyridylaminopyrimidine*.—The quaternary salt (III; $R^1 = R^2 = R^3 = H$) (0·5 g.) was refluxed for 2 hr. in ethanol (20 ml.) containing aniline (2 ml.). The solid slowly dissolved and after a short time the anilinopyrimidine began to separate. The 2-*anilinopyrimidine* crystallised from ethanol in yellow needles, m. p. 218° (Found : C, 59·6; H, 4·8; N, 25·7. $C_{16}H_{14}O_2N_6$ requires C, 59·6; H, 4·4; N, 26·1%). A better solvent for this reaction was 50% aqueous acetone. This pyrimidine could also be obtained by shaking the quaternary salt with ethanol and aniline at room temperature for 2 hr., or by heating the quaternary salt with aniline at 125° for 10 min.

2-*Amino*-6-*methyl*-5-*nitro*-4-2′-*pyridylaminopyrimidine*.—(*a*) The quaternary salt (III; $R^2 = R^3 = H$, $R^1 = Me$) (1 g.) was heated at 100° in saturated methanolic ammonia (25 ml.) in a sealed tube for 1 hr. The solution was cooled and the solid was collected. The product crystallised from butan-1-ol as yellow prisms, m. p. 230° alone or mixed with the compound prepared as follows.

(*b*) 2-Amino-4-chloro-6-methyl-5-nitropyrimidine (Boon *et al.*, *loc. cit.*) (0·2 g.) and 2-aminopyridine (0·4 g.) were heated at 125° for ½ hr. The melt was triturated with ethanol, the solid was filtered off, and 2-*amino*-6-*methyl*-5-*nitro*-4-2′-*pyridylaminopyrimidine* crystallised from butan-1-ol (m. p. 230°) (Found : C, 49·0; H, 4·5; N, 33·9. $C_{10}H_{10}O_2N_6$ requires C, 48·8; H, 4·1; N, 34·1%).

Reaction of 2 : 4-*Dichloro*-5-*nitropyrimidine with* 2-*Amino*-6-*methylpyridine*.—(a) *With* 2 *mols. of* 2-*amino*-6-*methylpyridine*. Solutions of 2-amino-6-methylpyridine (1·9 g.) in methanol 20 (ml.) and of 2 : 4-dichloro-5-nitropyrimidine (2 g.) in methanol (20 ml.) were mixed and set aside for 2 hr. at 0°. The precipitate was crystallised from ethanol, to give 2-*chloro*-4-(6-*methyl*-2-*pyridylamino*)-5-*nitropyrimidine* (2 g.) in yellow needles, m. p. 144° (Found : C, 45·2; H, 3·35; N, 25·7. $C_{10}H_8O_2N_5Cl$ requires C, 45·2; H, 3·0; N, 26·4%).

(b) *With* 4 *mols. of* 2-*amino*-6-*methylpyridine*. After the reactants had been boiled in methanol for 5 hr. and then cooled, the precipitate was crystallised from glacial acetic acid, to give 2 : 4-*di*-(6-*methyl*-2-*pyridylamino*)-5-*nitropyrimidine*, m. p. 318°, yellow needles (Found : C, 56·9; H, 4·5; N, 28·8. $C_{16}H_{15}O_2N_7$ requires C, 57·0; H, 4·5; N, 29·1%).

Reaction of 2 : 4-*Dichloro*-5-*nitropyrimidine with* 2-*Amino*-3-*methylpyridine*.—When this reaction was carried out in methanol solution at 0° with 2—3 mols. of the pyridine the only product was the *salt* (III; $R^1 = H$, $R^2 = Me$, $R^3 = H$) which crystallised from water in yellow prisms, m. p. 250° (decomp.) (Found : C, 51·4; H, 4·5; N, 26·6. $C_{16}H_{16}O_2N_7Cl$ requires C, 51·4; H, 4·3; N, 26·4%).

If one mol. of the dichloro-compound was refluxed with 4 mols. of 2-amino-3-methylpyridine in boiling methanol solution the product was 2-*methoxy*-4-(3-*methyl*-2-*pyridylamino*)-5-*nitropyrimidine* which crystallised from water [or, better, light petroleum (b. p. 40—60°)] as yellow prisms, m. p. 110° (Found: C, 50·4; H, 4·5; N, 26·9. $C_{11}H_{11}O_3N_5$ requires C, 50·6; H, 4·2; N, 26·8%).

Reaction of 2 : 4-*Dichloro*-5-*nitropyrimidine with* 2-*Amino*-4-*methylpyridine*.—The dichloro-compound was treated with 3 mols. of the base in ice-cold methanol to give the *salt* (III; $R^1 = R^2 = H$, $R^3 = Me$), m. p. 237—238° (decomp.), yellow prisms (from water) (Found: C, 51·7; H, 4·6; N, 26·0. $C_{16}H_{16}O_2N_7Cl$ requires C, 51·4; H, 4·3; N, 26·2%).

When the dichloropyrimidine was refluxed with 4 mols. of 2-amino-4-methylpyridine in hot methanol 2-*methoxy*-4-(4-*methyl*-2-*pyridylamino*)-5-*nitropyrimidine* was obtained as yellow prisms (from butan-1-ol), m. p. 180° (Found: C, 50·65; H, 4·35; N, 27·3. $C_{11}H_{11}O_3N_5$ requires C, 50·6; H, 4·2; N, 26·8%).

Reaction of 2 : 4-*Dichloro*-6-*methyl*-5-*nitropyrimidine with* 2-*Amino*-6-*methylpyridine*.—(*a*) The dichloropyrimidine (2·08 g.) was dissolved in ether (30 ml.), and 2-amino-6-methylpyridine (2·16 g.) in methanol (30 ml.) was added. After 1 hr. at 0° the ether was removed and the solution was diluted with water, giving 2-*chloro*-6-*methyl*-4-(6-*methyl*-2-*pyridylamino*)-5-*nitropyrimidine* (2 g.), m. p. 120°, yellow needles (from ethanol) (Found: C, 46·8; H, 3·8; N, 24·0. $C_{11}H_{10}O_2N_5Cl$ requires C, 47·2; H, 3·6; N, 25·05%).

(*b*) The dichloropyrimidine was refluxed with 4 mols. of 2-amino-6-methylpyridine in methanol, to give 6-*methyl*-2 : 4-*di*-(6-*methyl*-2-*pyridylamino*)-5-*nitropyrimidine*, m. p. 180°, yellow needles (from ethanol) (Found: C, 58·2; H, 5·05. $C_{17}H_{17}O_2N_7$ requires C, 58·1; H, 4·9%).

Reaction of 6-*Amino*-2 : 4-*dichloro*-5-*nitropyrimidine with* 2-*Aminopyridine*.—(*a*) Keeping 6-amino-2 : 4-dichloro-5-nitropyrimidine (1 g.) and 2-aminopyridine (1·4 g., 3 mols.) in acetone (30 ml.) for 4 days at room temperature, evaporating the solution and extracting the residual solid with hot water gave a residue A (0·3 g.). The hot aqueous filtrate was treated with charcoal, filtered, and cooled; a solid B (1 g.) separated.

Solid A, crystallised from butan-1-ol, gave 6-*amino*-2-*chloro*-4-2′-*pyridylamino*-5-*nitropyrimidine* as yellow needles, m. p. 239° (Found: C, 40·8; H, 2·8; N, 31·8. $C_9H_7O_2N_6Cl$ requires C, 40·5; H, 2·65; N, 31·5%).

Solid B, crystallised from ethanol–ether, yielded the *chloride* (III; $R^1 = NH_2$, $R^2 = R^3 = H$) as yellow prisms, m. p. 271° (decomp.) (Found: C, 46·3; H, 3·7; N, 30·4. $C_{14}H_{13}O_2N_8Cl$ requires C, 46·6; H, 3·6; N, 31·1%). The *iodide* crystallised from water in orange prisms, m. p. 265° (decomp.) (Found: C, 37·3; H, 3·3; N, 25·0. $C_{14}H_{13}O_2N_8I$ requires C, 37·2; H, 2·9; N, 24·8%).

(*b*) Reaction with 2 mols. of 2-aminopyridine in ice-cold ethanol gave only 6-amino-2-chloro-4-2′-pyridylamino-5-nitropyrimidine, m. p. and mixed m. p. 239°.

Preparation of Quaternary Salts from 2-*Chloropyrimidines*.—2-Chloro-5-nitro-4-2′-pyridylaminopyrimidine (0·5 g.), dissolved in hot benzene (25 ml.) and treated with pyridine (0·7 ml.), gave, on cooling, 1-(5-*nitro*-4-2′-*pyridylamino*-2-*pyrimidyl*)*pyridinium chloride* (V; R^2 = 2′-pyridylamino, $R^1 = R^3 = H$, A = Cl) (0·6 g.) as a yellow semi-crystalline solid which crystallised from ethanol–ether in yellow prisms, m. p. 220° (decomp.) (dependent on rate of heating) (Found: C, 51·2; H, 3·35; N, 25·1. $C_{14}H_{11}O_2N_6Cl$ requires C, 50·8; H, 3·35; N, 25·4%).

To a solution of 4-anilino-2-chloro-5-nitropyrimidine (0·3 g.) in hot benzene (20 ml.) was added pyridine (0·5 ml.). An aqueous solution of the salt, precipitated on cooling, was treated with a saturated solution of sodium iodide; the *pyridinium iodide* (0·2 g.) (V; $R^2 = Ph{\cdot}NH$, $R^1 = R^3 = H$, A = I) separated. It crystallised from water in orange plates, m. p. 215° (decomp.) (Found: C, 42·2; H, 3·2; N, 17·0. $C_{15}H_{12}O_2N_5I$ requires C, 42·9; H, 2·9; N, 16·7%).

2-Chloro-4-(6-methyl-2-pyridylamino)-5-nitropyrimidine and pyridine in benzene yielded the *chloride* (V; R^2 = 6-methyl-2-pyridylamino, $R^1 = R^3 = H$, A = Cl), yellow needles (from ethanol–ether), m. p. 200° (decomp.) (Found: C, 52·4; H, 4·2; N, 24·4. $C_{15}H_{13}O_2N_6Cl$ requires C, 52·2; H, 3·8; N, 24·4%).

When 2-chloro-6-methyl-4-(6-methyl-2-pyridylamino)-5-nitropyrimidine and pyridine were mixed in hot benzene solution a dark solid was obtained. This was extracted with water (charcoal), and the pale yellow extract, treated with a saturated solution of sodium iodide, gave the *quaternary iodide* (V; R^2 = 6-methyl-2-pyridylamino, R^1 = Me, $R^3 = H$, A = I), scarlet needles (from water), m. p. 224° (decomp.) (Found: C, 42·9; H, 4·5; N, 19·1. $C_{16}H_{15}O_2N_6I$ requires C, 42·7; H, 3·4; N, 18·7%).

The *salt* (V; $R^2 = NH_2$, $R^1 = R^3 = H$, A = Cl) was prepared from the components in acetone and crystallised from ethanol–ether in buff needles, m. p. 255—256° (decomp.) (Found : C, 42·0; H, 3·5; N, 27·45. $C_9H_8O_2N_5Cl$ requires C, 42·6; H, 3·2; N, 27·6%). Similarly were prepared the *chlorides* (V; $R^2 = R^3 = NH_2$, $R^1 = H$, A = Cl), pale orange-yellow rods (from water), m. p. 273—274° (decomp.) (Found : C, 40·7; H, 3·5; N, 31·1. $C_9H_9O_2N_6Cl$ requires C, 40·2; H, 3·4; N, 31·35%), (V; $R^2 = Ph{\cdot}NH$, $R^1 = H$, $R^3 = NH_2$, A = Cl), yellow prisms (from ethanol–ether), m. p. 200—202° (decomp.) (Found : C, 51·8; H, 4·2; N, 23·9. $C_{15}H_{13}O_2N_6Cl$ requires C, 52·2; H, 3·8; N, 24·4%), and (V; R^2 = 6-methyl-2-pyridylamino, $R^1 = H$, $R^3 = NH_2$, A = Cl), yellow prisms (from ethanol–ether), m. p. 222—223° (decomp.) (Found : C, 49·8; H, 4·3; N, 27·7. $C_{13}H_{14}O_2N_7Cl$ requires C, 50·1; H, 3·9; N, 27·3%).

The *iodides* corresponding to the last two crystallised from water in orange rods, m. p. 213—214° (decomp.) (Found : C, 41·3; H, 2·7; N, 19·9. $C_{15}H_{13}O_2N_6I$ requires C, 41·3; H, 3·0; N, 19·3%), and orange needles, m. p. 252° (decomp.) (Found : C, 39·6; H, 2·3; N, 21·1. $C_{13}H_{14}O_2N_7I$ requires C, 39·9; H, 3·1; N, 21·7 %),respectively.

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