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

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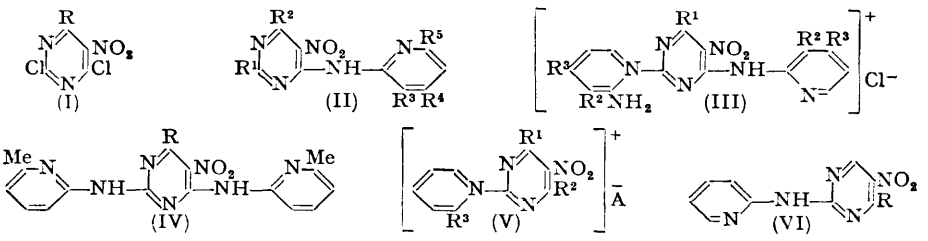
[Reprint Order No. 6146.]

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 amino-pyridyl 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′-pyridylaminopyrimidine* (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. $C_{14}H_{12}O_2N_7Cl$ 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·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.

We thank Professor A. Haddow for his interest and encouragement, and Mrs. K. Tussler for the analyses. This investigation has been supported by grants to this Institute from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund, and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service.

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