73. *Synthetic Antimalarials. Part VI. Some 4-Arylamino-2-aminoalkylamino-6-methylpyrimidines.*

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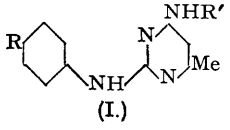
The investigation of pyrimidine derivatives carrying aminoalkylamino side chains as antimalarials (Parts I—V, this vol., pp. 343—366) has been extended to include a number of 4-arylamino-2-aminoalkylamino-6-methylpyrimidines. Both the arylamino and aminoalkylamino groups have been varied.

The structure of these compounds is discussed in connection with certain hypotheses which attempt to relate chemical constitution and antimalarial activity.

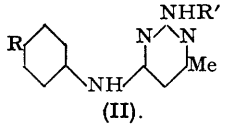
Most of the compounds were made by condensation of 4-hydroxy-2-methylthio-6-methylpyrimidine with an aminoalkylamine to give a 2-aminoalkylamino-4-hydroxy-6-methylpyrimidine, followed by replacement of hydroxyl by chlorine and condensation with an arylamine. 4-*p*-Chloroanilino-2-aminoalkylamino-6-methylpyrimidines were made also by condensing 2-*chloro*-4-p-*chloroanilino*-6-*methylpyrimidine* with an aminoalkylamine at the last stage. The 2-chloro-4-*p*-chloroanilino-6-methylpyrimidine was synthesised from 4-chloro-2-methylthio-6-methylpyrimidine by condensation with *p*-chloroaniline, desulphurisation of the resulting 4-p-*chloroanilino*-2-*methylthio*-6-*methylpyrimidine* to the corresponding 2-*hydroxy* compound, and replacement of hydroxyl by chlorine.

Some of the compounds showed high antimalarial activity against *P. gallinaceum* in chicks.

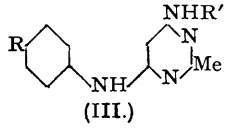
Following the discovery of antimalarial activity in compounds of the type (I; R = Cl, OMe, R′ = $[CH_2]_n$·N(dialkyl)$_2$) (Part I, Curd and Rose, this vol., p. 343) it was of obvious importance to examine compounds of the two possible isomeric structures (II) and (III). In this paper an account is given of the preliminary work carried out on compounds of type (II) in which the positions of the substituted anilino and aminoalkylamino residues in (I) are interchanged.



(I.)



(II).



(III.)

The formal resemblance to riboflavin exhibited by compounds of type (I) is shared by substances of type (II), and since the type (I) can function as riboflavin antagonists (Madinaveitia, *Biochem. J.*, in the press) it was anticipated that type (II) would behave similarly. Therefore, on the basis of the hypothesis that the antimalarial activity of type (I) is dependent on a riboflavin antagonism (see Curd, Davey, and Rose, *Ann. Trop. Med. Parasit.*, in the press), it seemed likely that compounds of type (II) might also display antimalarial properties.

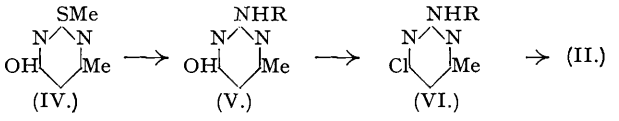
The hypothesis of Schönhöfer (*Z. physiol. Chem.*, 1942, **274**, 1) relating antimalarial activity to the possibility of the formation of a *p*-quinonoid structure in the molecule was confined to quinoline and acridine derivatives, but on the basis of our work on compounds of type (I) (Part I, *loc. cit.*) it appeared as if it might also be applicable to pyrimidine derivatives provided that other structural requirements were satisfied.

The inactivity of 2-aminoalkylamino-6-methoxyquinolines (Schönhöfer, *loc. cit.*; Magidson and Rubtsov, *J. Gen. Chem. Russ.*, 1937, **7**, 1896) would appear to exclude *o*-quinonoid tautomerism from any significance as regards antimalarial activity. It has, however, been suggested in Part V (Curd, Raison, and Rose, this vol., p. 366) that the activity of the 4-dialkylaminoalkylamino-6-methoxyquinolines is due to their structural relationship to mepacrine and that they may act in the same way, possibly by interference with some riboflavin-containing enzyme essential to the malaria parasites. On structural grounds it is difficult to see how the isomeric 2-dialkylaminoalkylamino compounds can act in this way, and it is therefore conceivable that their inactivity may be due to inability to function as riboflavin antagonists rather than to the fact that tautomerism to give a *p*-quinonoid structure is not possible

Compounds of type (II) are likewise incapable of exhibiting the *p*-quinonoid type of tautomerism, the aminoalkylamino group not being in the *para* position to either of the heterocyclic nitrogen atoms, and this circumstance appeared to offer an excellent opportunity of examining the scope, if not the validity, of the Schönhöfer hypothesis. It seemed possible, for instance, that for antimalarial activity in quinoline, acridine, and pyrimidine derivatives the Schönhöfer requirements had to be met in addition to a formal resemblance to riboflavin.

Preliminary experiments having shown that the replacement of one of the two chlorine atoms in 2 : 4-dichloro-6-methylpyrimidine by either arylamino or aminoalkylamino groups led to mixtures of isomers, the separation of which was difficult, a method of synthesis was sought which would obviate this. Such a method, which is illustrated schematically below, was suggested by the work of Johnson and Mackenzie (*Amer. Chem. J.*, 1909, **42**, 353) who reported that methylamine condensed with 4-hydroxy-2-methylthio-6-methylpyrimidine (IV) to give 2-methylamino-4-hydroxy-6-methylpyrimidine (V; R = Me) which was converted into 4-chloro-2-methylamino-6-methylpyrimidine (VI; R = Me) by the action of phosphoryl chloride. When (IV) was heated with β-diethylaminoethylamine at 160—170° a rapid evolution of methylthiol occurred which was complete in about 2 hours and left 2-β-*diethylaminoethylamino*-4-*hydroxy*-6-*methylpyrimidine* (V; R = $[CH_2]_2{\cdot}NEt_2$) as a colourless resin, easily soluble in water, which was characterised as its *dipicrate*. Short refluxing with phosphoryl chloride was sufficient to convert (V; R = $[CH_2]_2{\cdot}NEt_2$) into 4-*chloro*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine* (VI; R = $[CH_2]_2{\cdot}NEt_2$) which was purified by high vacuum distillation. This compound, like the others of this type described below, was stable in presence of water, either neutral or alkaline, but decomposed fairly rapidly under acid conditions, presumably owing to activation of the chlorine atom in a manner analogous to that suggested by Banks (*J. Amer. Chem. Soc.*, 1944, **66**, 1127, 1131).

(VI; R = $[CH_2]_2{\cdot}NEt_2$) condensed with *p*-chloroaniline hydrochloride (one molecular proportion) in presence of *p*-chloroaniline (excess) at 160—170° to give directly 4-p-*chloroanilino*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine dihydrochloride* (II; R = Cl, R′ = $[CH_2]_2{\cdot}NEt_2$). This was separated from unchanged starting materials by repeated extraction with benzene and purified by crystallisation from methanol, a procedure designed in order to facilitate isolation directly as a dihydrochloride.



After some of the compounds described below had been prepared it was discovered that the condensation of compounds of type (VI) with arylamine hydrochlorides proceeded rapidly in boiling water or aqueous acetone, a little free hydrochloric acid usually being added as a catalyst. The products often crystallised from the reaction mixture as their dihydrochlorides in an almost pure condition. The corresponding bases (not always isolated) were either colourless viscous oils or solids of fairly low m. p. Using this method (VI; R = $[CH_2]_2{\cdot}NEt_2$) was condensed with aniline and a number of substituted anilines to provide a series of compounds (II) having different substituents in the anilino residue. The following were used : aniline, *p*-toluidine, *p*-anisidine, *p*-cyanoaniline, *p*-nitroaniline, and 3 : 4-dichloroaniline.

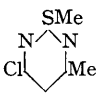
The second part of our original plan for the investigation of compounds of type (II) was to examine the effect of varying the aminoalkylamino side chain in position 2 while having a *p*-chloroanilino group in position 4. The *p*-chloroanilino group was selected because our previous work on compounds of type (I) (Part I, *loc. cit.*; Part II, Curd, Davis, and Rose, this vol., p. 351) had indicated that highest antimalarial activity was obtained with the chlorine substituent and it was anticipated that, if both types of compound acted by a common mechanism, the effects of different substituents would probably be roughly parallel in the two series.

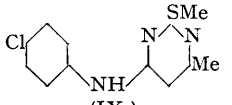
Utilising the method of synthesis outlined above the following 6-methylpyrimidines were therefore prepared as their *dihydrochlorides* : 4-p-*chloroanilino*-2-γ-*diethylaminopropylamino*- (II; R = Cl, R′ = $[CH_2]_3{\cdot}NEt_2$) through the intermediate stages (V; R = $[CH_2]_3{\cdot}NEt_2$) and (VI; R = $[CH_2]_3{\cdot}NEt_2$); 4-p-*chloroanilino*-2-γ-*dimethylaminopropylamino*- (II; R = Cl, R′ = $[CH_2]_3{\cdot}NMe_2$) through (V; R = $[CH_2]_3{\cdot}NMe_2$) and (VI; R = $[CH_2]_3{\cdot}NMe_2$); 4-p-*chloroanilino*-2-γ-*di*-n-*butylaminopropylamino*- (II; R = Cl, R′ = $[CH_2]_3{\cdot}NBu^{\alpha}_2$) through (V; R = $[CH_2]_3{\cdot}NBu^{\alpha}_2$), and (VI; R = $[CH_2]_3{\cdot}NBu^{\alpha}_2$); 4-p-*chloroanilino*-2-δ-*diethylaminobutylamino*- (II; R = Cl, R′ = $[CH_2]_4{\cdot}NEt_2$) through (V; R = $[CH_2]_4{\cdot}NEt_2$) and (VI; R = $[CH_2]_4{\cdot}NEt_2$); and 4-p-*chloroanilino*-2-δ-*diethylamino*-α-*methylbutylamino*- (II; R = Cl, R′ = $CHMe{\cdot}[CH_2]_3{\cdot}NEt_2$) through (V; R = $CHMe{\cdot}[CH_2]_3{\cdot}NEt_2$) and (VI; R = $CHMe{\cdot}[CH_2]_3{\cdot}NEt_2$). In addition to the above dialkylaminoalkylamino compounds we also prepared 4-p-*chloroanilino*-2-γ-*piperidinopropylamino*-6-*methylpyrimidine* (II; R = Cl, R′ = $[CH_2]_3{\cdot}N{<}[CH_2]_4{>}CH_2$), through (V; R = $[CH_2]_3{\cdot}N{<}[CH_2]_4{>}CH_2$) and (VI; R = $[CH_2]_3{\cdot}N{<}[CH_2]_4{>}CH_2$) and 4-p-*chloroanilino*-2-γ-n-*butylaminopropylamino*-6-*methylpyrimidine* (II; R = Cl, R′ = $[CH_2]_3{\cdot}NHBu^{\alpha}$) through (V; R = $[CH_2]_3{\cdot}NHBu^{\alpha}$) and (VI; R = $[CH_2]_3{\cdot}NHBu^{\alpha}$).

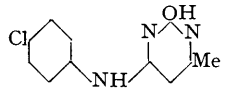
The results of antimalarial tests (see table) on these compounds indicated that the effect of variations of the basic side chain was entirely different from that which had obtained in the isomeric series (I) and that further variations would be desirable. For this purpose an alternative method of synthesis, involving only one new stage in each case, was investigated.

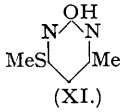
Johnson, Johns, and Heyl (*Amer. Chem. J.*, 1906, **36**, 177) condensed 4-chloro-2-methylthiopyrimidine with arylamines (*e.g.*, with *p*-toluidine to give 4-*p*-toluidino-2-methylthiopyrimidine which was hydrolysed with hydrochloric acid to 4-*p*-toluidino-2-hydroxypyrimidine). The corresponding reaction of 4-chloro-2-methylthio-6-methylpyrimidine (VIII) with *p*-chloroaniline and desulphurisation of the product was therefore tried. The condensation of (VIII) and *p*-chloroaniline to give (IX) took place either at 120° in acetic acid or in boiling aqueous acetone in presence of a catalytic amount of hydrochloric acid. Hydrolysis of (IX) to 4-p-*chloroanilino*-2-*hydroxy*-6-*methylpyrimidine* could not be easily accomplished by boiling with hydrochloric acid, but with 48% hydrobromic acid desulphurisation proceeded smoothly and the hydrolysis product (X) was isolated in good yield.

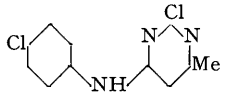
The same compound was also obtained by condensing 2-hydroxy-4-methylthio-6-methylpyrimidine (XI) (Wheeler and McFarland, *Amer. Chem. J.*, 1909, **42**, 421) with *p*-chloroaniline at 120—130°, thus providing confirmatory evidence that the effect of the hydrobromic acid treatment of (IX) had been limited to the methylthio group. Treatment of (X) with phosphoryl chloride converted it into the corresponding chloro compound (XII) from which the following were again prepared by condensation with the appropriate aminoalkylamines; (II; R = Cl, R′ = $[CH_2]_2$·NEt_2), (II; R = Cl, R′ = $[CH_2]_3$·NEt_2), (II; R = Cl, R′ = $[CH_2]_3$·$NHBu^{\alpha}$), and (II; R = Cl, R′ = $[CH_2]_3$·NBu^{α}_2), all of which were isolated as their dihydrochlorides. The products were identical with those prepared by the original method.

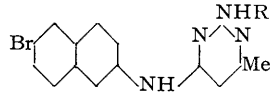

(VIII.)


(IX.)


(X.)


(XI.)


(XII.)

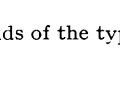

(XIII.)

This method, which was an exact parallel to that used in Parts I and II (*loc. cit.*) for the preparation of the isomeric 2-arylamino-4-aminoalkylamino-6-methylpyrimidines, was then employed for the preparation of the following 6-methylpyrimidines: 4-p-*chloroanilino*-2-*γ-dimethylaminobutylamino*- (II; R = Cl, R′ = $[CH_2]_4$·NMe_2), 4-*p*-chloroanilino-2-δ-dibutylaminobutylamino- (*dihydrochloride*) (II; R = Cl, R′ = $[CH_2]_4$·NBu^{α}_2), 4-*p*-chloroanilino-2-methyl*iso*propylaminopropylamino- (*dihydrochloride*) (II; R = Cl, R′ = $[CH_2]_3$·$NMePr^{\beta}$) and 4-*p*-chloroanilino-2-δ-diamylaminopropylamino- (*dihydrochloride*) (II; R = Cl, R′ = $[CH_2]_3$·$N(C_5H_{11}{}^{\alpha})_2$).

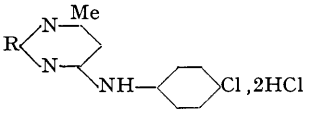
In view of the high activity exhibited by 2-(6′-bromo-β-naphthylamino)-4-β-diethylaminoethylamino-6-methylpyrimidine against *P. gallinaceum* in chicks (see Part V, *loc. cit.*) it was thought advisable to include in this initial study of compounds of type (II) a number of substances of the general formula (XIII). By condensation of 6-bromo-β-naphthylamine with the appropriate variant of (VI) the following 6-methylpyrimidines were obtained as *dihydrochlorides*: 4-(6′-bromo-β-naphthylamino)-2-β-diethylaminoethylamino- (XIII; R = $[CH_2]_2$·NEt_2), 4-(6′-bromo-β-naphthylamino)-2-γ-diethylaminopropylamino- (XIII; R = $[CH_2]_3$·NEt_2), 4-(6′-bromo-β-naphthylamino)-2-γ-dibutylaminopropylamino- (XIII; R = $[CH_2]_3$·NBu^{α}_2), 4-(6′-bromo-β-naphthylamino)-2-δ-diethylamino-α-methylbutylamino- (XIII; R = CHMe·$[CH_2]_3$·NEt_2), 4-(6′-bromo-β-naphthylamino)-2-γ-piperidinopropylamino- (XIII; R = $[CH_2]_3$·N < $[CH_2]_4$ > CH_2) and 4-(6′-bromo-β-naphthylamino)-2-γ-*n*-butylaminopropylamino- (XIII; R = $[CH_2]_3$·$NHBu^{\alpha}$).

Antimalarial activities.

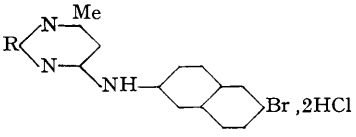
The tests referred to were carried out against *P. gallinaceum* in chicks and the method of expressing antimalarial activity is the same as that used in Part I. Full biological results will be published elsewhere.

(*a*) Compounds of the type Et_2N·$[CH_2]_2$·NH—  ,2HCl

Ref. No.	Nature of R.	Dose, mg./kg.	Activity.	Ref. No.	Nature of R.	Dose, mg./kg.	Activity.
3883	4′-Chloroanilino	120	+	3888	Anilino	160	—
		80	+			80	—
		40	—	4317	4′-Nitroanilino	120	++
3885	4′-Toluidino	160	—			80	+
		40	—			40	—
3886	4′-Anisidino	160	—	4346	4′-Cyanoanilino	160	++
		40	—			80	+ to ++
3887	3′ : 4′-Dichloroanilino	200	—			40	+
		40	—				

(*b*) Compounds of the type 

3743	NH·[CH$_2$]$_3$·NEt$_2$	120	++	4508	NH·[CH$_2$]$_3$·NHBu$^\alpha$	40	+ to ++
		80	++			20	−
		40	+	4190	NH·[CH$_2$]$_3$·N<[CH$_2$]$_4$>CH$_2$	80	++
4561	NH·[CH$_2$]$_4$·NEt$_2$	240	++			40	+
		120	+ to ++	4316	NH·[CH$_2$]$_3$·NBu$^\alpha_2$	80	++
		80	+ to ++			40	++
		40	−			20	+
5052	NH·CHMe·[CH$_2$]$_3$·NEt$_2$ [1]	80	−	4786	NH·[CH$_2$]$_3$·NMePr$^\beta$	40	+
		40	−	4668	NH·[CH$_2$]$_4$·NMe$_2$ [2]	40	−
4345	NH·[CH$_2$]$_3$·NMe$_2$	160	++	4669	NH·[CH$_2$]$_4$·NBu$^\alpha_2$	80	++
		80	++			40	±
		40	+	5149	NH·[CH$_2$]$_3$·N(C$_5$H$_{11}^\alpha$)$_2$	80	++
		20	−			20	±

(*c*) Compounds of the type 

3884	NH·[CH$_2$]$_2$·NEt$_2$	80	−	5063	NH·CHMe·[CH$_2$]$_3$·NEt$_2$	80	−
		40	−			40	−
4787	NH·[CH$_2$]$_3$·NEt$_2$	80	±	5041	NH·[CH$_2$]$_3$·N<[CH$_2$]$_4$>CH$_2$	80	+
		40	−			40	−
4788	NH·[CH$_2$]$_3$·NBu$^\alpha_2$	80	+ to ++	5152	NH·[CH$_2$]$_3$·NHBu$^\alpha$	80	−
		60	−				
		40	−				

[1] Dihydrobromide. [2] Base.

Experimental.

2-β-*Diethylaminoethylamino*-4-*hydroxy*-6-*methylpyrimidine* (V; R = [CH$_2$]$_2$·NEt$_2$).—4-Hydroxy-2-methylthio-6-methylpyrimidine (31·2 g.) was heated with β-diethylaminoethylamine (23·2 g.) at 160—180° for 3 hours leaving the product as a nearly colourless resin which could not be induced to crystallise. The corresponding *dipicrate* crystallised from β-ethoxyethanol in yellow laminæ, m. p. 178—180° (Found: C, 40·0; H, 3·8; N, 20·1. C$_{11}$H$_{20}$ON$_4$,2C$_6$H$_3$O$_7$N$_3$ requires C, 40·5; H, 3·8; N, 20·5%).

4-*Chloro*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine* (VI; R = [CH$_2$]$_2$·NEt$_2$).—The above hydroxy compound (44·8 g.) and phosphoryl chloride (100 c.c.) were boiled for 5 minutes and the cooled reaction mixture poured on ice. The resulting solution was made alkaline with sodium hydroxide and the precipitated oil extracted with benzene. The benzene solution was washed once with water and then extracted twice with 5% acetic acid. The combined extracts were immediately made alkaline with sodium hydroxide and the product again taken into benzene. After drying over solid sodium hydroxide and removing the solvent the residual oil was distilled, giving 4-*chloro*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine* as a colourless oil, b. p. 140°/0·1 mm., which solidified on standing to colourless needles, m. p. 33° (yield, 59%) (Found: Cl, 14·6. C$_{11}$H$_{19}$N$_4$Cl requires Cl, 14·6%). The *dipicrate*, prepared in methanol solution, formed yellow prisms from β-ethoxyethanol, m. p. 158—159° (Found: C, 39·7; H, 4·2; N, 19·7; Cl, 4·8. C$_{11}$H$_{19}$N$_4$Cl,2C$_6$H$_3$O$_7$N$_3$ requires C, 39·4; H, 3·6; N, 20·0; Cl, 5·1%).

4-p-*Chloroanilino*-2-*methylthio*-6-*methylpyrimidine* (IX).—(a) 4-Chloro-2-methylthio-6-methylpyrimidine (13 g.) (Wheeler and McFarland, *Amer. Chem. J.*, 1909, **42**, 431), *p*-chloroaniline (9·6 g.), and glacial acetic acid (100 c.c.) were mixed, 7 drops of concentrated hydrochloric acid added, and the mixture heated on the steam-bath for ½ hr. After cooling, the crystals which had been deposited were filtered off, suspended in alcohol, and treated with ammonia. Addition of water precipitated the product, which was filtered off, washed with water, and crystallised from alcohol. 4-p-*Chloroanilino*-2-*methylthio*-6-*methylpyrimidine* (yield, 15·2 g.) formed colourless rhombic prisms, m. p. 171—172° (Found: C, 54·0; H, 4·5; S, 12·5. C$_{12}$H$_{12}$N$_3$ClS requires C, 54·25; H, 4·5; S, 12·1%). The *picrate* crystallised from β-ethoxyethanol, m. p. 226° (Found: N, 16·6; Cl, 7·8. C$_{12}$H$_{12}$N$_3$ClS,C$_6$H$_3$O$_7$N$_3$ requires N, 17·0; Cl, 7·2%).

(b) 4-Chloro-2-methylthio-6-methylpyrimidine (8·7 g.), *p*-chloroaniline (6·4 g.), water (40 c.c.), and acetone (10 c.c.) were mixed, 10N-hydrochloric acid (0·5 c.c.) added, and the mixture refluxed for 1 hour. After cooling, the solid which had separated was filtered off and washed with water. It was then suspended in alcohol, made alkaline with ammonia, and the mixture diluted with water. Crystallisation of the resulting product from alcohol gave the same compound as (a) above, m. p. and mixed m. p. 170—172°.

4-p-*Chloroanilino*-2-*hydroxy*-6-*methylpyrimidine* (X).—(a) 2-Hydroxy-4-methylthio-6-methylpyrimidine (15·6 g.) and *p*-chloroaniline (37·5 g.) were heated at 160—170° for 3 hours. Methylthiol was evolved and, after cooling, the solid melt was ground, boiled with alcohol, and filtered. After refluxing with β-ethoxyethanol, the *product* (20 g.) was collected as a white crystalline powder, m. p. >330° (Found: N, 18·3; Cl, 15·0. C$_{11}$H$_{10}$ON$_3$Cl requires N, 17·8; Cl, 15·1%).

(b) 4-*p*-Chloroanilino-2-methylthio-6-methylpyrimidine (36 g.) and 48% hydrobromic acid (360 c.c.) were refluxed for 24 hours. The resulting clear solution was diluted with water, made alkaline with ammonia, and the precipitated product filtered off. For purification it was dissolved in aqueous-alcoholic sodium hydroxide, and the solution filtered and acidified with acetic acid. 4-*p*-Chloroanilino-2-hydroxy-6-methylpyrimidine was thus obtained as colourless prisms, which were filtered off, washed with water, and dried at 100° (yield, 30 g.), m. p. >330° (Found: Cl, 15·0%).

2-*Chloro*-4-p-*chloroanilino*-6-*methylpyrimidine* (XII).—The above hydroxy compound (32 g.) and phosphoryl chloride (75 c.c.) were refluxed for 3 hours. The resulting mixture was poured on ice with stirring and, after the ice had melted, made alkaline with ammonia. The solid was filtered off, suspended in alcohol, ammonia added until alkaline, and the resulting solution poured into water. The product separated as an oil which soon crystallised. It was filtered off,

dried, and crystallised from methanol giving 2-*chloro*-4-p-*chloroanilino*-6-*methylpyrimidine* as colourless thick prisms, m. p. 136—137° (yield, 19·4 g.) (Found: C, 52·2; H, 3·5; N, 16·5. $C_{11}H_9N_3Cl_2$ requires C, 52·0; H, 3·5; N, 16·5%).

4-p-*Chloroanilino*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine* (II; R = Cl, R′ = $[CH_2]_2{\cdot}NEt_2$).—(a) 4-Chloro-2-β-diethylaminoethylamino-6-methylpyrimidine (4·85 g.), *p*-chloroaniline (7·68 g.), and *p*-chloraniline hydrochloride (3·3 g.) were mixed and heated at 175—185° for 2 hours. After cooling, benzene (50 c.c.) was added and the mixture stirred well to dissolve excess of *p*-chloroaniline. The undissolved material was filtered off, washed with hot benzene, and dried. It was then dissolved in water (30 c.c.), sodium acetate (1 g.) and acetic acid (1 c.c.) added, and the solution boiled for a short time with decolorising charcoal. After filtering and cooling, the filtrate was salted out with sodium chloride. The crystalline precipitate of 4-p-*chloroanilino*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine dihydrochloride* (3883) was filtered off. It crystallised from methanol as colourless cubes, m. p. 265—267° (yield, 3·0 g.) (Found: C, 47·0; H, 6·6; N, 16·7; Cl, 24·8; Cl′, 16·7. $C_{17}H_{24}N_5Cl,2HCl,1{\cdot}5H_2O$ requires C, 47·1; H, 6·7; N, 16·2; Cl, 24·6; Cl′, 16·4%).

(b) 4-Chloro-2-β-diethylaminoethylamino-6-methylpyrimidine (18·3 g.), *p*-chloroaniline (9·6 g.), water (75 c.c.) and 10N-hydrochloric acid (7·5 c.c.) were refluxed for 1 hour. The reaction mixture was then cooled, made alkaline with sodium hydroxide, and extracted with chloroform. The chloroform solution was shaken several times with 5% acetic acid, the combined acetic acid extracts made alkaline with sodium hydroxide, and the base taken into chloroform. After drying (K_2CO_3) and removal of the solvent the residual oil was distilled in a vacuum, b. p. 193—200°/0·65 mm. It then crystallised from light petroleum (b. p. 80—100°), giving 4-p-*chloroanilino*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine* as colourless tables, m. p. 97° (Found: C, 61·1; H, 7·3; Cl, 10·7. $C_{17}H_{24}N_5Cl$ requires C, 61·2; H, 7·2; Cl, 10·6%). The *dipicrate* crystallised from β-ethoxyethanol as flat yellow prisms, m. p. 227—228° (Found: C, 43·6; H, 3·8; N, 19·8; Cl, 4·8. $C_{17}H_{24}N_5Cl,2C_6H_3O_7N_3$ requires C, 44·0; H, 3·8; N, 19·5; Cl, 4·5%).

(c) 2-Chloro-4-*p*-chloroanilino-6-methylpyrimidine (12·7 g.) and β-diethylaminoethylamine (7·2 g.) were mixed and heated at 120—130° for 8 hours. The cooled reaction mixture was dissolved in dilute hydrochloric acid, made alkaline with sodium hydroxide, and worked up as described under (b) above. The resulting crude base was dissolved in hot 2N-hydrochloric acid. On cooling, the dihydrochloride crystallised out and was filtered off and dried. It crystallised from alcohol as colourless needles, m. p. 266—268° either alone or admixed with material made by method (a) (Found: C, 48·6; H, 6·5; N, 16·5; Cl′, 17·2. $C_{17}H_{24}N_5Cl,2HCl,H_2O$ requires C, 48·0; H, 6·6; N, 16·5; Cl′, 16·8%).

4-p-*Toluidino*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine* (II; R = Me, R′ = $[CH_2]_2{\cdot}NEt_2$).—(a) A mixture of 4-chloro-2-β-diethylaminoethylamino-6-methylpyrimidine (4·85 g.), *p*-toluidine (6·42 g.), and *p*-toluidine hydrochloride (2·87 g.) was heated at 180—190° for 1¾ hours. The cooled reaction mixture was triturated with benzene, and the insoluble material filtered off and dried. Crystallisation from methanol and then from pentanol gave 4-p-*toluidino*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine dihydrochloride* (3885) as colourless prisms, m. p. 236—238° (Found: C, 54·0; H, 7·5; N, 17·0; Cl′, 18·3. $C_{18}H_{27}N_5,2HCl,H_2O$ requires C, 53·5; H, 7·7; N, 17·3; Cl′, 17·6%).

(b) 4-Chloro-2-β-diethylaminoethylamino-6-methylpyrimidine (3·0 g.), *p*-toluidine (1·35 g.), water (15 c.c.), and 10N-hydrochloric acid (1·25 c.c.) were refluxed for 1 hour. The reaction mixture was cooled, made alkaline with sodium hydroxide, and extracted with chloroform. The chloroform extract was extracted several times with 5% acetic acid, the acid extracts combined, and sodium hydroxide added. The liberated *base*, isolated with chloroform, crystallised from light petroleum (b. p. 80—100°) as colourless prisms, m. p. 66—68° (Found: C, 68·6; H, 8·5; N, 22·0. $C_{18}H_{27}N_5$ requires C, 69·0; H, 8·6; N, 22·4%). The *dipicrate* crystallised from β-ethoxyethanol as yellow prisms, m. p. 191—193° (Found: C, 47·3; H, 4·4; N, 19·4. $C_{18}H_{27}N_5,2C_6H_3O_7N_3$ requires C, 46·7; H, 4·3; N, 20·0%).

4-p-*Anisidino*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine* (II; R = OMe, R′ = $[CH_2]_2{\cdot}NEt_2$).—4-Chloro-2-β-diethylaminoethylamino-6-methylpyrimidine (4·85 g.), *p*-anisidine (7·38 g.), and *p*-anisidine hydrochloride (3·19 g.) were heated at 160—170° for 2 hours and worked up with benzene as described above. Crystallisation of the resulting crude product from *n*-propanol gave 4-p-*anisidino*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine dihydrochloride* (3886) as colourless needles, m. p. 216—218° (Found: C, 49·3; H, 7·4; N, 16·4; Cl′, 16·9. $C_{18}H_{27}ON_5,2HCl,2H_2O$ requires C, 49·3; H, 7·5; N, 16·0; Cl′, 16·2%). The *dipicrate* formed thick yellow rectangular prisms from β-ethoxyethanol, m. p. 180° (Found: C, 45·6; H, 4·2; N, 19·2. $C_{18}H_{27}ON_5,2C_6H_3O_7N_3$ requires C, 45·75; H, 4·2; N, 19·6%).

4-*Anilino*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine* (II; R = H, R′ = $[CH_2]_2{\cdot}NEt_2$).—In an analogous manner 4-chloro-2-β-diethylaminoethylamino-6-methylpyrimidine (4·85 g.), aniline (5·58 g.), and aniline hydrochloride (2·59 g.) gave 4-*anilino*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine dihydrochloride* (3888) as colourless thick prisms (from methanol), m. p. 238° (Found: C, 50·0; H, 7·5; N, 17·1; Cl′, 17·6. $C_{17}H_{25}N_5,2HCl,2H_2O$ requires C, 50·0; H, 7·6; N, 17·2; Cl′, 17·4%). The *monopicrate monohydrochloride* prepared from the dihydrochloride with picric acid in methanol solution crystallised from β-ethoxyethanol as flat yellow prisms, m. p. 228° (Found: C, 48·9; H, 4·9; N, 19·7; Cl, 6·1. $C_{17}H_{25}N_5,HCl,C_6H_3O_7N_3$ requires C, 48·9; H, 5·1; N, 19·8; Cl, 6·3%).

4-(3′:4′-*Dichloroanilino*)-2-β-*diethylaminoethylamino*-6-*methylpyrimidine*.—The *dihydrochloride* (3887) prepared in a similar manner from 4-chloro-2-β-diethylaminoethylamino-6-methylpyrimidine (4·0 g.), 3:4-dichloroaniline (5·35 g.), and 3:4-dichloroaniline hydrochloride (3·28 g.) crystallised from methanol as colourless prisms, m. p. 260—261° (Found: C, 44·9; H, 5·7; N, 15·8; Cl′, 15·6. $C_{17}H_{23}N_5Cl_2,2HCl,H_2O$ requires C, 44·4; H, 5·9; N, 15·3; Cl′, 15·5%). The *dipicrate* separated from β-ethoxyethanol as flat yellow prisms, m. p. 218—219° (Found: C, 42·1; H, 3·7; N, 18·7. $C_{17}H_{23}N_5Cl_2,2C_6H_3O_7N_3$ requires C, 42·1; H, 3·5; N, 18·7%).

4-p-*Cyanoanilino*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine* (4346) (II; R = CN, R′ = $[CH_2]_2{\cdot}NEt_2$).—4-Chloro-2-β-diethylaminoethylamino-6-methylpyrimidine (3·9 g.), *p*-cyanoaniline (3·8 g.), and *p*-cyanoaniline hydrochloride (2·5 g.) were mixed and heated at 175° for 1 hour. After cooling, the reaction mixture was boiled with benzene (25 c.c.) and the solid product filtered off. After three further similar treatments with boiling benzene the solid was crystallised from methanol. It formed colourless prisms, m. p. 307—308° (yield, 1·9 g.) (Found: C, 53·5; H, 6·4; N, 20·9; Cl, 17·2. $C_{18}H_{24}N_6,2HCl,0{\cdot}5H_2O$ requires C, 53·2; H, 6·5; N, 20·2; Cl, 17·1%).

4-p-*Nitroanilino*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine* (II; R = NO_2, R′ = $[CH_2]_2{\cdot}NEt_2$).—(a) 4-Chloro-2-β-diethylaminoethylamino-6-methylpyrimidine (7·3 g.), *p*-nitroaniline (13·4 g.), and *p*-nitroaniline hydrochloride (5·1 g.) were mixed and heated at 185° for 3 hours. Repeated extraction of the reaction mixture with hot benzene left a solid which was crystallised from water. 4-p-*Nitroanilino*-2-β-*diethylaminoethylamino*-6-*methylpyrimidine dihydrochloride* (4317) was thereby obtained as yellowish needles, m. p. 293° (decomp.) (Found: C, 48·7; H, 6·2; N, 19·4; Cl′, 16·9. $C_{17}H_{24}O_2N_6,2HCl$ requires C, 48·9; H, 6·2; N, 20·1; Cl′, 17·0%).

(b) 4-Chloro-2-β-diethylaminoethylamino-6-methylpyrimidine (8·1 g.), *p*-nitroaniline (4·6 g.), water (40 c.c.), and 10N-hydrochloric acid (3·3 c.c.) were refluxed for 2 hours and the product worked up as described above for the corresponding *p*-toluidino compound (method (b)). The *base* was thereby obtained as yellow prisms from benzene, m. p. 161—162° (yield, 7·7 g.) (Found: C, 59·7; H, 7·1; N, 24·2. $C_{17}H_{24}O_2N_6$ requires C, 59·3; H, 7·0; N, 24·4%).

2-γ-*Diethylaminopropylamino*-4-*hydroxy*-6-*methylpyrimidine* (V; R = $[CH_2]_3{\cdot}NEt_2$).—4-Hydroxy-2-methylthio-6-methylpyrimidine (7·8 g.) and γ-diethylaminopropylamine (6·5 g.) were heated at 160—180° for 3 hours. Methylthiol was evolved and the product remained as a colourless, extremely viscous oil, soluble in water and the usual organic solvents. It could not be obtained crystalline and was therefore characterised as its *dipicrate* which separated from

β-ethoxyethanol in yellow laminæ, m. p. 211—212° (Found : C, 41·8; H, 4·2; N, 19·7. $C_{12}H_{22}ON_4,2C_6H_3O_7N_3$ requires C, 41·3; H, 4·0; N, 20·1%).

4-*Chloro*-2-γ-*diethylaminopropylamino*-6-*methylpyrimidine* (VI; R = $[CH_2]_3{\cdot}NEt_2$).—The above hydroxypyrimidine (11·9 g.) and phosphoryl chloride (25 c.c.) were gradually heated to boiling when a brisk reaction set in, the hydroxy compound passing into solution. Refluxing was continued for 5 minutes. The reaction mixture was then rapidly cooled and poured on ice. The resulting deep yellow solution was made alkaline with sodium hydroxide. The oil thereby precipitated was taken up in benzene, and the benzene solution washed with water and then extracted with 5% acetic acid. The combined acetic acid extracts were immediately made alkaline with sodium hydroxide, the precipitated product extracted with chloroform, and the dried (Na_2SO_4) extract evaporated. The oil was purified by distillation giving 4-*chloro*-2-γ-*diethylaminopropylamino*-6-*methylpyrimidine* (yield, 78%), b. p. 142°/0·05 mm. (Found : Cl, 13·2. $C_{12}H_{21}N_4Cl$ requires Cl, 13·8%). The *dipicrate* crystallised from β-ethoxyethanol as yellow prisms, m. p. 157—159° (Found : C, 41·1; H, 4·1; N, 19·2; Cl, 4·5. $C_{12}H_{21}N_4Cl,2C_6H_3O_7N_3$ requires C, 40·3; H, 3·8; N, 19·6; Cl, 5·0%).

4-p-*Chloroanilino*-2-γ-*diethylaminopropylamino*-6-*methylpyrimidine* (II; R = Cl, R′ = $[CH_2]_3{\cdot}NEt_2$).—(a) 4-Chloro-2-γ-diethylaminopropylamino-6-methylpyrimidine (5·2 g.), *p*-chloroaniline (7·68 g.), and *p*-chloroaniline hydrochloride (3·3 g.) were mixed and heated at 165—170° (oil-bath) for 2 hours. The product was worked up as described above for the corresponding preparation of 4-*p*-chloroanilino-2-β-diethylaminoethylamino-6-methylpyrimidine dihydrochloride. Crystallised from methanol–ethyl acetate, 4-p-*chloroanilino*-2-γ-*diethylaminopropylamino*-6-*methylpyrimidine dihydrochloride* (3743) formed long colourless prisms, m. p. 269—271° (Found : C, 47·7; H, 6·7; N, 15·6; Cl′, 16·2. $C_{18}H_{26}N_5Cl,2HCl,2H_2O$ requires C, 47·4; H, 7·0; N, 15·3; Cl′, 15·6%). Addition of picric acid to its solution in methanol gave a *monopicrate monohydrochloride* which separated from β-ethoxyethanol as flat yellow prisms, m. p. 236—238° (Found : C, 47·2; H, 4·6; N, 17·7; Cl, 12·1. $C_{18}H_{26}N_5Cl,HCl,C_6H_3O_7N_3$ requires C, 47·0; H, 4·9; N, 18·25; Cl, 11·6%).

(b) 4-Chloro-2-γ-diethylaminopropylamino-6-methylpyrimidine (6·4 g.), *p*-chloroaniline (3·2 g.), water (25 c.c.), and 10N-hydrochloric acid (2·5 c.c.) were refluxed for 1 hour. The product which separated on cooling was filtered off, dried, and crystallised from alcohol–ethyl acetate giving 4-*p*-chloroanilino-2-γ-diethylaminopropylamino-6-methylpyrimidine dihydrochloride (yield, 7·7 g.), m. p. 268—270° undepressed by material made by method (a). The *dipicrate* crystallised from β-ethoxyethanol as thick yellow prisms, m. p. 213—214° (Found : C, 44·4; H, 4·1; N, 18·7; Cl, 4·9. $C_{18}H_{26}N_5Cl,2C_6H_3O_7N_3$ requires C, 44·7; H, 4·0; N, 19·1; Cl, 4·4%).

(c) 2-Chloro-4-*p*-chloroanilino-6-methylpyrimidine (5 g.) and γ-diethylaminopropylamine (3·2 g.) were heated at 120—130° (oil-bath) for 8 hours. The cooled mixture was dissolved in warm dilute hydrochloric acid, and the solution filtered from a small amount of insoluble matter, cooled, and made alkaline with sodium hydroxide. The liberated base was taken into chloroform and the solution extracted with 5% acetic acid. The acid extract was made alkaline with sodium hydroxide and the base again extracted with chloroform. After removal of the solvent the base was converted into the dihydrochloride by dissolving in hot 2N-hydrochloric acid, cooling, collecting, and drying. It formed long colourless prisms from methanol–ethyl acetate, m. p. 268—270° alone or mixed with material made by method (a).

2-γ-*Dimethylaminopropylamino*-4-*hydroxy*-6-*methylpyrimidine* (V; R = $[CH_2]_3{\cdot}NMe_2$).—4-Hydroxy-2-methylthio-6-methylpyrimidine (31·2 g.) and γ-dimethylaminopropylamine (20·4 g.) were mixed and heated to 160° in 1 hour, then kept at 160—180° for 3 hours. On cooling, the product was a practically colourless resin. It formed a *dipicrate* which crystallised from β-ethoxyethanol in yellow laminæ, m. p. 201—202° (Found : C, 39·8; H, 3·8; N, 20·7. $C_{10}H_8ON_4,2C_6H_3O_7N_3$ requires C, 39·5; H, 3·6; N, 21·0%).

4-*Chloro*-2-γ-*dimethylaminopropylamino*-6-*methylpyrimidine* (VI; R = $[CH_2]_3{\cdot}NMe_2$).—The above hydroxypyrimidine (42 g.) and phosphoryl chloride (100 c.c.) were gradually heated to boiling when a vigorous reaction occurred and the hydroxypyrimidine rapidly passed into solution. After refluxing for 5 minutes and working up in the usual way 4-*chloro*-2-γ-*dimethylaminopropylamino*-6-*methylpyrimidine* was obtained as a colourless oil, b. p. 120—122°/0·1 mm. (slight decomp.) (Found : C, 53·0; H, 7·8; N, 25·5; Cl, 14·4. $C_{10}H_{17}N_4Cl$ requires C, 52·5; H, 7·4; N, 24·5; Cl, 15·5%). The compound decomposed slowly on standing but gave satisfactory results in condensations with arylamines if used soon after preparation. The *dipicrate* crystallised from alcohol as thick yellow prisms, m. p. 146—147° (Found : C, 38·9; H, 3·4; N, 20·5. $C_{10}H_{17}N_4Cl,2C_6H_3O_7N_3$ requires C, 38·5; H, 3·4; N, 20·4%).

4-p-*Chloroanilino*-2-γ-*dimethylaminopropylamino*-6-*methylpyrimidine* (4345) (II; R = Cl, R′ = $[CH_2]_3{\cdot}NMe_2$).—4-Chloro-2-γ-dimethylaminopropylamino-6-methylpyrimidine (4·0 g.), *p*-chloroaniline (6·7 g.), and *p*-chloroaniline hydrochloride (2·9 g.) were heated at 165—170° for 3 hours. The cooled mixture was stirred with benzene (125 c.c.) for 1 hour. By decantation of the benzene and repetition of the process a *solid* was obtained which crystallised from methanol as colourless thick prisms, m. p. 270° (Found : C, 49·0; H, 6·0; N, 17·9; Cl, 27·1. $C_{16}H_{22}N_5Cl,2HCl$ requires C, 48·9; H, 6·1; N, 17·8; Cl, 27·1%).

2-γ-*Dibutylaminopropylamino*-4-*hydroxy*-6-*methylpyrimidine* (V; R = $[CH_2]_3{\cdot}NBu^{\alpha}_2$).—4-Hydroxy-2-methylthio-6-methylpyrimidine (23·4 g.) and γ-di-*n*-butylaminopropylamine (27·9 g.) were heated at 160—180° for 3 hours. The *product* was a practically colourless very viscous oil which did not crystallise. The *dipicrate* separated from methanol in thick yellow laminæ, m. p. 224—225° (Found : C, 44·8; H, 4·9; N, 18·6. $C_{16}H_{30}ON_4,2C_6H_3O_7N_3$ requires C, 44·7; H, 4·8; N, 18·6%).

4-*Chloro*-2-γ-*dibutylaminopropylamino*-6-*methylpyrimidine* (VI; R = $[CH_2]_3{\cdot}NBu^{\alpha}_2$).—The above hydroxypyrimidine (44·1 g.) and phosphoryl chloride (75 c.c.) were gradually heated to boiling when a reaction took place, the hydroxy compound passing into solution. After boiling for 10 minutes, 30 c.c. of phosphoryl chloride were removed under reduced pressure at 40° and the residue was worked up in the usual manner. 4-*Chloro*-2-γ-*dibutylaminopropylamino*-6-*methylpyrimidine* was thereby obtained as a practically colourless oil (30 g.) which did not distil below 190°/0·2 mm. It was characterised as its *dipicrate* which formed flat yellow needles from β-ethoxyethanol–alcohol, m. p. 156—157° (Found : C, 43·7; H, 4·7; N, 17·8. $C_{16}H_{29}N_4Cl,2C_6H_3O_7N_3$ requires C, 43·6; H, 4·5; N, 18·2%).

4-p-*Chloroanilino*-2-γ-*dibutylaminopropylamino*-6-*methylpyrimidine* (II; R = Cl, R′ = $[CH_2]_3{\cdot}NBu^{\alpha}_2$).—(a) 4-Chloro-2-γ-dibutylaminopropylamino-6-methylpyrimidine (7·1 g.), *p*-chloroaniline (9·3 g.), and *p*-chloroaniline hydrochloride (4·1 g.) were mixed and heated at 165—170° for 3 hours. The resulting melt was stirred with benzene (125 c.c.) for 1 hour, the benzene decanted off, and the process repeated thrice. The solid product was crystallised from methanol and then from methanol–acetone giving 4-p-*chloroanilino*-2-γ-*dibutylaminopropylamino*-6-*methylpyrimidine dihydrochloride* (4316), m. p. 169—171° (Found in material dried at 80° : C, 53·5; H, 7·4; N, 13·8; Cl′, 14·9. $C_{22}H_{34}N_5Cl,2HCl,H_2O$ requires C, 53·4; H, 7·7; N, 14·2; Cl′, 14·4%). The *dipicrate* crystallised from β-ethoxyethanol–alcohol as yellow prisms, m. p. 220—222° (Found : C, 47·0; H, 4·8; Cl, 4·4. $C_{22}H_{34}N_5Cl,2C_6H_3O_7N_3$ requires C, 47·4; H, 4·5; Cl, 4·2%).

(b) 4-Chloro-2-γ-dibutylaminopropylamino-6-methylpyrimidine (7·8 g.), *p*-chloroaniline (3·2 g.), water (25 c.c.), and 10N-hydrochloric acid (2·5 c.c.) were boiled for 1 hour. The product, which crystallised out on cooling, was filtered off and dried. It crystallised from alcohol–ethyl acetate as colourless thick prisms, m. p. 171—173° undepressed by

material made by method (a) (Found in air-dried material : C, 51·8; H, 7·3; N, 13·4; Cl′, 13·3. $C_{22}H_{34}N_5Cl,2HCl,2H_2O$ requires C, 51·5; H, 7·8; N, 13·7; Cl′, 13·8%).

(c) 2-Chloro-4-*p*-chloroanilino-6-methylpyrimidine (10 g.) and γ-di-*n*-butylaminopropylamine (9·2 g.) were mixed and heated at 120—130° for 8 hours. The mixture was worked up as described above for 4-*p*-chloroanilino-2-γ-diethylaminopropylamino-6-methylpyrimidine (method (c)) giving the base as an oil which was converted into the dihydrochloride by dissolving in hot 2N-hydrochloric acid. The salt, which separated on cooling, was filtered off, dried, and crystallised from alcohol–ethyl acetate; it had m. p. 171—173°, not depressed by admixture with material made by method (b) (Found in air-dried material : C, 51·6; H, 7·9; N, 13·9%).

2-δ-*Diethylaminobutylamino*-4-*hydroxy*-6-*methylpyrimidine* (V; R = $[CH_2]_4{\cdot}NEt_2$).—4-Hydroxy-2-methylthio-6-methylpyrimidine (15·6 g.) and δ-diethylaminobutylamine (14·4 g.) were heated at 160—180° for 3 hours. A rapid evolution of methylthiol took place at first but gradually subsided leaving the base as a pale yellow highly viscous oil which crystallised on long standing. The *dipicrate* formed thick yellow prisms from β-ethoxyethanol, m. p. 209° (Found : C, 42·6; H, 4·2; N, 20·5. $C_{13}H_{24}ON_4,2C_6H_3O_7N_3$ requires C, 42·3; H, 4·2; N, 19·7%).

4-*Chloro*-2-δ-*diethylaminobutylamino*-6-*methylpyrimidine* (VI; R = $[CH_2]_4{\cdot}NEt_2$).—The preceding hydroxypyrimidine (25·2 g.) and phosphoryl chloride (50 c.c.) were heated, and, when the vigorous reaction had subsided, the reaction was completed by refluxing for 5 minutes. The mixture was drowned into sodium hydroxide (500 c.c. of 5N), toluene (250 c.c.), and ice. The toluene layer was separated and the aqueous layer extracted with toluene (250 c.c.). The combined toluene extracts were rapidly extracted thrice with ice-cold 5% acetic acid. The aqueous extracts were combined, poured into excess of ice-cold 5N-sodium hydroxide, and the product extracted with chloroform. Evaporation of the dried (Na_2SO_4) chloroform solution left the base as an oil (yield, 76%). The *dipicrate* crystallised from β-ethoxyethanol as thick yellow prisms, m. p. 146° (Found : N, 19·3; Cl, 4·5. $C_{13}H_{23}N_4Cl,2C_6H_3O_7N_3$ requires N, 19·2; Cl, 4·9%).

4-p-*Chloroanilino*-2-δ-*diethylaminobutylamino*-6-*methylpyrimidine* (II; R = Cl, R′ = $[CH_2]_4{\cdot}NEt_2$).—4-Chloro-2-δ-diethylaminobutylamino-6-methylpyrimidine (5·5 g.), *p*-chloroaniline (7·68 g.), and *p*-chloroaniline hydrochloride (3·3 g.) were heated at 150—160° for 2 hours. The reaction mixture was triturated four times with hot benzene (20 c.c.), and the residue dissolved in water (25 c.c.) with the addition of acetic acid (2 c.c.) and sodium acetate (2 g.), and extracted thrice with benzene (25 c.c.). The aqueous layer was separated, clarified with decolorising charcoal, and filtered. Addition of sodium hydroxide to the filtrate precipitated the product which was extracted with chloroform and dried (Na_2SO_4). Evaporation of the solvent left the base as an oil which did not crystallise. With picric acid in methanol it gave a *dipicrate* which crystallised from β-ethoxyethanol as flat yellow prisms, m. p. 226—227° (Found : C, 45·4; H, 4·4; N, 18·6; Cl, 4·2. $C_{19}H_{28}N_5Cl,2C_6H_3O_7N_3$ requires C, 45·4; H, 4·2; N, 18·8; Cl, 4·3%). The base was converted into its *dihydrochloride* by stirring with water and sufficient hydrochloric acid to render the mixture acid to Congo red. The salt was filtered off and crystallised from aqueous methanol, being thus obtained as colourless thick prisms, m. p. 197—198° (Found : C, 48·2; H, 7·3; N, 15·3; Cl′, 14·8. $C_{19}H_{28}N_5Cl,2HCl,2H_2O$ requires C, 48·5; H, 7·2; N, 14·9; Cl′, 15·1%) (4561).

2-δ-*Diethylamino*-α-*methylbutylamino*-4-*hydroxy*-6-*methylpyrimidine* (V; R = $CHMe{\cdot}[CH_2]_3{\cdot}NEt_2$).—4-Hydroxy-2-methylthio-6-methylpyrimidine (31·2 g.) and δ-diethylamino-α-methylbutylamine (31·6 g.) were mixed and heated at 160—180° for 3 hours. Methylthiol was evolved leaving a non-crystallisable resin. It formed a *dipicrate* which crystallised from β-ethoxyethanol–alcohol in irregular yellow laminæ, m. p. 170—172° (Found : C, 43·7; H, 4·5; N, 18·7. $C_{14}H_{26}ON_4,2C_6H_3O_7N_3$ requires C, 43·1; H, 4·4; N, 19·3%).

4-*Chloro*-2-δ-*diethylamino*-α-*methylbutylamino*-6-*methylpyrimidine* (VI; R = $CHMe{\cdot}[CH_2]_3{\cdot}NEt_2$).—2-δ-Diethylamino-α-methylbutylamino-4-hydroxy-6-methylpyrimidine (53·2 g.) and phosphoryl chloride (100 c.c.) were gradually heated to 100°. When the vigorous reaction had subsided the mixture was refluxed for 5 minutes. Some of the excess of phosphoryl chloride (*ca.* 40 c.c.) was then removed under reduced pressure at 40° and the residue poured on crushed ice (500 g.). The resulting solution was immediately made alkaline with sodium hydroxide and extracted several times with benzene. After washing the benzene solution with water the product was extracted by shaking several times with 5% acetic acid. The combined acid extracts were added to excess of sodium hydroxide solution and the product taken into benzene. Evaporation of the dried benzene solution gave 4-*chloro*-2-δ-*diethylamino*-α-*methylbutylamino*-6-*methylpyrimidine* as a colourless oil, b. p. 142°/0·07 mm. (yield, 45·7%) (Found : C, 59·4; H, 8·8; N, 19·8; Cl, 12·3. $C_{14}H_{25}N_4Cl$ requires C, 59·0; H, 8·8; N, 19·7; Cl, 12·5%). The *dipicrate* separated from methanol in thick yellow laminæ, m. p. 148—149° (Found : C, 41·9; H, 4·0; N, 19·0; Cl, 5·0. $C_{14}H_{25}N_4Cl,2C_6H_3O_7N_3$ requires C, 42·0; H, 4·2; N, 18·9; Cl, 4·8%).

4-p-*Chloroanilino*-2-δ-*diethylamino*-α-*methylbutylamino*-6-*methylpyrimidine* (II; R = Cl, R′ = $CHMe{\cdot}[CH_2]_3{\cdot}NEt_2$).—The above chloropyrimidine (14·2 g.), *p*-chloroaniline (6·35 g.), water (50 c.c.), and 10N-hydrochloric acid (4·4 c.c.) were refluxed for 3 hours. The resulting clear solution was made alkaline with sodium hydroxide and the liberated base extracted with chloroform. The chloroform solution was then extracted several times with 5% acetic acid, the acid extracts combined and made alkaline with sodium hydroxide, and the base again taken up into chloroform. Evaporation of the dried (K_2CO_3) extract and distillation of the residue gave 4-p-*chloroanilino*-2-δ-*diethylamino*-α-*methylbutylamino*-6-*methylpyrimidine*, b. p. 220—223°/0·15 mm. (yield, 9·5 g.) (Found : C, 63·5; H, 7·5; N, 18·6. $C_{20}H_{30}N_5Cl$ requires C, 63·9; H, 7·9; N, 18·6%). The *dipicrate* crystallised from β-ethoxyethanol–alcohol in clusters of small yellow needles, m. p. 189—190° (Found : C, 45·6; H, 4·3; N, 18·0. $C_{20}H_{30}N_5Cl,2C_6H_3O_7N_3$ requires C, 46·0; H, 4·3; N, 18·5%).

The dihydrochloride could not be crystallised satisfactorily and the *dihydrobromide* (5052) was therefore prepared for biological testing. The base was dissolved in dilute hydrobromic acid and the solution evaporated to dryness at 60—65° under reduced pressure. The residue was freed from water and excess of hydrobromic acid by repeated evaporation to dryness under reduced pressure with alcohol and alcohol–benzene. It then crystallised from alcohol–ethyl acetate as colourless flat prisms, m. p. 200—201° (Found : C, 44·6; H, 5·9; N, 12·9; Br′, 29·0. $C_{20}H_{30}N_5Cl,2HBr$ requires C, 44·7; H, 6·0; N, 13·0; Br′, 29·8%).

2-γ-*Piperidinopropylamino*-4-*hydroxy*-6-*methylpyrimidine* (V; R = $[CH_2]_3{\cdot}N{<}[CH_2]_4{>}CH_2$).—4-Hydroxy-2-methylthio-6-methylpyrimidine (23·4 g.) and γ-piperidinopropylamine (21·3 g.) were heated at 160—180° for 3 hours. Methylthiol was evolved with effervescence leaving a practically colourless very viscous oil. With water it formed a *hydrate* which crystallised from water in practically colourless prisms, m. p. 81—82° (Found in air-dried material : C, 54·4; H, 8·9; N, 19·8; loss at 100° in a vacuum, 12·1. $C_{13}H_{22}ON_4,2H_2O$ requires C, 54·5; H, 9·1; N, 19·6; H_2O, 12·6%). The *dipicrate* had m. p. 218° (Found : C, 42·5; H, 3·9; N, 19·7. $C_{13}H_{22}ON_4,2C_6H_3O_7N_3$ requires C, 42·4; H, 4·0; N, 19·8%).

4-*Chloro*-2-γ-*piperidinopropylamino*-6-*methylpyrimidine* (VI; R = $[CH_2]_3{\cdot}N{<}[CH_2]_4{>}CH_2$).—The above hydroxy compound (37·5 g.) and phosphoryl chloride (75 c.c.) were mixed and heated to 80—100° when a vigorous reaction ensued. After refluxing for ½ hour the mixture was distilled at 40° under reduced pressure until 30 c.c. of phosphoryl chloride had been removed. It was then worked up as described above for other compounds of this type giving 4-*chloro*-2-γ-*piperidinopropylamino*-6-*methylpyrimidine* as a colourless oil, b. p. 127°/0·04 mm. (yield, 17·5 g.), which

gradually solidified and then had m. p. 52—53° (Found : C, 58·1; H, 7·9; N, 20·4. $C_{13}H_{21}N_4Cl$ requires C, 58·1; H, 7·8; N, 20·9%). The *dipicrate*, prepared in methanol solution, crystallised from β-ethoxyethanol as thick yellow plates, m. p. 195° (Found : C, 41·3; H, 3·7; N, 19·0. $C_{13}H_{21}N_4Cl,2C_6H_3O_7N_3$ requires C, 41·3; H, 2·9; N, 19·3%).

4-p-*Chloroanilino*-2-γ-*piperidinopropylamino*-6-*methylpyrimidine* (II; R = Cl, R′ = $[CH_2]_3{\cdot}N<[CH_2]_4>CH_2$).—4-Chloro-2-γ-piperidinopropylamino-6-methylpyrimidine (10 g.), *p*-chloroaniline (15·9 g.), and *p*-chloroaniline hydrochloride (6·8 g.) were mixed and heated at 165—170° for 3 hours. The cooled reaction mixture was stirred with benzene and the crystalline product collected and washed with benzene. Crystallisation from methanol–ethyl acetate gave the *dihydrochloride* (4190) as colourless slender prisms, m. p. 277—279° (Found : C, 48·9; H, 6·5; N, 14·9; Cl′, 14·5. $C_{19}H_{26}N_5Cl,2HCl,2H_2O$ requires C, 48·7; H, 6·8; N, 14·9; Cl′, 15·1%).

2-γ-n-*Butylaminopropylamino*-4-*hydroxy*-6-*methylpyrimidine* (V; R = $[CH_2]_3{\cdot}NHBu^{\alpha}$).—4-Hydroxy-2-methylthio-6-methylpyrimidine (24 g.) and γ-*n*-butylaminopropylamine (20 g.) were heated at 160—180° for 3 hours. On cooling, the product was a very highly viscous oil. The *dipicrate* crystallised from alcohol as thick yellow needles, m. p. 200° (Found : C, 41·7; H, 4·2; N, 20·4. $C_{12}H_{22}ON_4,2C_6H_3O_7N_3$ requires C, 41·4; H, 4·0; N, 20·1%). The *dinitrobenzoate* had m. p. 193—194° (Found : C, 47·2; H, 4·5; N, 16·7. $C_{12}H_{22}ON_4,2C_7H_4O_6N_2$ requires C, 47·1; H, 4·5; N, 16·9%).

4-*Chloro*-2-γ-n-*butylaminopropylamino*-6-*methylpyrimidine* (VI; R = $[CH_2]_3{\cdot}NHBu^{\alpha}$).—The above hydroxypyrimidine (35 g.) and phosphoryl chloride (75 c.c.) were heated until a vigorous reaction occurred. When this had subsided the mixture was refluxed for 2 minutes (complete solution) and worked up as described above in similar cases. Evaporation of the final benzene extract left an oil (18·6 g.) which could not be distilled without decomposition. It also decomposed on keeping at room temperature to give a high melting solid, but, for condensation with arylamines, successful results were obtained by using the crude product immediately after preparation. No pure crystalline derivative could be obtained.

4-p-*Chloroanilino*-2-γ-n-*butylaminopropylamino*-6-*methylpyrimidine* (II; R = Cl, R′ = $[CH_2]_3{\cdot}NHBu^{\alpha}$).—(a) 4-Chloro-2-γ-*n*-butylaminopropylamino-6-methylpyrimidine (7·7 g. of crude product), *p*-chloroaniline (12·4 g.), and *p*-chloroaniline hydrochloride (5·2 g.) were mixed and heated at 160—170° for 1 hour. The mixture quickly became homogeneous and then began to deposit solid material. After cooling it was treated twice with boiling benzene and the insoluble material isolated by decantation. This was then dissolved in methanol (30 c.c.) and the solution poured into benzene (300 c.c.). The resulting crystalline product was further purified by crystallisation from methanol giving 4-p-*chloroanilino*-2-γ-n-*butylaminopropylamino*-6-*methylpyrimidine dihydrochloride* (4508) as colourless prisms, m. p. 301—303° (yield, 6·1 g.) (Found : C, 50·7; H, 6·7; N, 16·8; Cl′, 17·0. $C_{18}H_{26}N_5Cl,2HCl$ requires C, 51·4; H, 6·7; N, 16·7; Cl′, 16·9%).

(b) 2-Chloro-4-*p*-chloroanilino-6-methylpyrimidine (4·3 g.) and γ-*n*-butylaminopropylamine (8·2 g.) were heated at 120—130° for 8 hours, the resulting melt dissolved in warm dilute hydrochloric acid, and the solution made alkaline with sodium hydroxide. The liberated base was separated and extracted with 5% acetic acid, and the acid extract made alkaline and extracted with chloroform. After drying (K_2CO_3) and removal of the solvent, the product remained as an oil. The *dipicrate* crystallised from β-ethoxyethanol as yellow prisms, m. p. 205—206° (Found : C, 44·8; H, 4·1; N, 18·8. $C_{18}H_{26}N_5Cl,2C_6H_3O_7N_3$ requires C, 44·7; H, 4·0; N, 19·1%). The dihydrochloride, isolated from a solution of the base in 2N-hydrochloric acid by evaporation, crystallised from methanol–ethyl acetate as colourless needles, m. p. 300—302° undepressed by admixture with material made by method (a) above (Found : C, 50·9; H, 6·3; N, 16·9; Cl′, 16·2%).

4-p-*Chloroanilino*-2-δ-*dimethylaminobutylamino*-6-*methylpyrimidine* (II; R = Cl, R′ = $[CH_2]_4{\cdot}NMe_2$).—2-Chloro-4-*p*-chloroanilino-6-methylpyrimidine (12·7 g.) and δ-dimethylaminobutylamine (7·3 g.) were heated at 120—130° for 8 hours. The resulting viscous melt was heated with water, and sodium hydroxide added until alkaline to Clayton yellow. The liberated base was extracted with chloroform and the chloroform solution extracted several times with 5% acetic acid. Addition of sodium hydroxide to the combined acid extracts reprecipitated the base which was isolated with chloroform, and the chloroform solution dried and evaporated. By crystallisation of the residue, first from benzene and then from aqueous alcohol, 4-p-*chloroanilino*-2-δ-*dimethylaminobutylamino*-6-*methylpyrimidine* (4668) was obtained as colourless laminæ, m. p. 156—158° (Found : C, 61·0; H, 6·9; N, 20·9. $C_{17}H_{24}N_5Cl$ requires C, 61·2; H, 7·2; N, 21·0%). The *dipicrate* crystallised from β-ethoxyethanol as yellow needles, m. p. 205—207° (Found : C, 44·6; H, 3·9; N, 18·8. $C_{17}H_{24}N_5Cl$ requires C, 44·6; H, 3·9; N, 18·8%).

4-p-*Chloroanilino*-2-δ-*dibutylaminobutylamino*-6-*methylpyrimidine* (II; R = Cl, R′ = $[CH_2]_4{\cdot}NBu^{\alpha}_2$).—The base, prepared in a similar manner from 2-chloro-4-*p*-chloroanilino-6-methylpyrimidine (12·7 g.) and δ-dibutylaminobutylamine (12·5 g.), formed a practically colourless viscous oil, characterised as its *dipicrate* which crystallised from β-ethoxyethanol as yellow needles, m. p. 205—207° (Found : C, 48·6; H, 4·8; N, 17·7. $C_{23}H_{36}N_5Cl,2C_6H_3O_7N_3$ requires C, 48·0; H, 4·8; N, 17·6%). Its *dihydrochloride* (4669), prepared for biological test by dissolving in 2N-hydrochloric acid, evaporating the solution under reduced pressure, and crystallising the dried residue from alcohol–ethyl acetate, formed colourless needles, m. p. 125—127° (m. p. 147—149° immediately after drying at 100°) (Found in material dried at 100° : C, 53·7; H, 7·5; N, 13·8; Cl′, 14·0. $C_{23}H_{36}N_5Cl,2HCl,H_2O$ requires C, 54·3; H, 7·8; N, 13·7; Cl′, 13·7%).

4-p-*Chloroanilino*-2-*methyl*iso*propylaminopropylamino*-6-*methylpyrimidine* (II; R = Cl, R′ = $[CH_2]_3{\cdot}NMePr^{\beta}$).—The base, prepared similarly using γ-methyl*iso*propylaminopropylamine, formed a practically colourless oil which was not obtained crystalline. Its *dipicrate* crystallised from β-ethoxyethanol as yellow plates, m. p. 224—226° (Found : C, 45·1; H, 3·9; N, 18·9. $C_{18}H_{26}N_5Cl,2C_6H_3O_7N_3$ requires C, 44·7; H, 4·0; N, 19·1%). The *dihydrochloride* (4786) crystallised from alcohol as colourless needles, m. p. 274—276° (efferv.) (Found : C, 51·4; H, 6·5; N, 16·6; Cl′, 16·5. $C_{18}H_{26}N_5Cl,2HCl$ requires C, 51·4; H, 6·7; N, 16·65; Cl′, 16·9%).

4-p-*Chloroanilino*-2-γ-*di*-n-*amylaminopropylamino*-6-*methylpyrimidine* (II; R = Cl, R′ = $[CH_2]_3{\cdot}N(C_5H_{11}{}^{\alpha})_2$).—4-Chloro-2-*p*-chloroanilino-6-methylpyrimidine (7·6 g.) and γ-di-*n*-amylaminopropylamine (6·4 g.) were fused at 120°. After about 5 minutes' heating the melt, which was at first fluid, began to crystallise and gradually solidified. Heating at 120—130° was continued for 2 hours; the reaction mixture was then dissolved out with dilute hydrochloric acid, and the filtered solution made alkaline with sodium hydroxide and the liberated base separated. The oil was extracted twice with 5% acetic acid, and the extracts combined and treated with sodium hydroxide. The liberated base was extracted with chloroform, the extract dried with potassium carbonate and evaporated, leaving the base as an oil which did not crystallise. It gave a *dipicrate* which crystallised from β-ethoxyethanol in rosettes of small yellow needles, m. p. 210—212° (Found : C, 48·9; H, 5·0; N, 17·0. $C_{24}H_{38}N_5Cl,2C_6H_3O_7N_3$ requires C, 48·6; H, 4·95; N, 17·3%), and a *dihydrochloride* (5149) which crystallised from alcohol–ethyl acetate as colourless thick laminæ, m. p. 135—136° (Found : C, 54·3, 54·4; H, 7·7, 8·0; N, 13·0, 13·2; Cl′, 14·1. $C_{24}H_{38}N_5Cl,2HCl,1{\cdot}5H_2O$ requires C, 54·2; H, 8·1; N, 13·2; Cl′, 13·4%).

4-(6′-*Bromo*-β-*naphthylamino*)-2-β-*diethylaminoethylamino*-6-*methylpyrimidine* (XIII; R = $[CH_2]_2{\cdot}NEt_2$).—(a) 4-Chloro-2-β-diethylaminoethylamino-6-methylpyrimidine (4·5 g.), 6-bromo-β-naphthylamine (6·2 g.), and 6-bromo-β-naphthylamine hydrochloride (4·8 g.) were mixed, and heated at 180—190° for 2 hours. After cooling, the solid melt was ground, boiled with benzene, and filtered, and the insoluble residue was dried, then dissolved in water, filtered, and reprecipitated by hydrochloric acid. The resulting 4-(6′-*bromo*-β-*naphthylamino*)-2-β-*diethylaminoethylamino*-6-*methylpyrimidine dihydrochloride* (3884) was filtered off, dried, and recrystallised from methanol, forming colourless flat

prisms, m. p. 265—267° (yield, 5·1 g.) (Found : C, 47·0; H, 6·0; N, 13·5; Cl′, 13·3. $C_{21}H_{26}N_5Br,2HCl,2H_2O$ requires C, 46·9; H, 6·0; N, 13·0; Cl′, 13·2%). The *dipicrate* crystallised from β-ethoxyethanol as yellow laminæ, m. p. 224—225° (Found : C, 44·7; H, 4·3; N, 16·6. $C_{21}H_{26}N_5Br,2C_6H_3O_7N_3$ requires C, 44·7; H, 3·6; N, 17·3%).

(b) 4-Chloro-2-β-diethylaminoethylamino-6-methylpyrimidine (6·1 g.), 6-bromo-β-naphthylamine (5·5 g.), water (25 c.c.), and 10N-hydrochloric acid (2·5 c.c.) were refluxed for 1 hour. From the clear solution 4-(6′-bromo-β-naphthylamino)-2-β-diethylaminoethylamino-6-methylpyrimidine dihydrochloride crystallised on cooling. It was filtered off and dissolved in hot water, and the solution decolorised with charcoal and filtered. Addition of hydrochloric acid to the filtrate reprecipitated the product, which was filtered off, dried, and crystallised from alcohol. It formed colourless needles, m. p. 266—268° undepressed by admixture with material made by method (a) (yield, 9·9 g.).

4-(6′-*Bromo-β-naphthylamino*)-2-γ-*diethylaminopropylamino*-6-*methylpyrimidine* (XIII; R = $[CH_2]_3{\cdot}NEt_2$).—4-Chloro-2-γ-diethylaminopropylamino-6-methylpyrimidine (6·4 g.), 6-bromo-β-naphthylamine (5·5 g.), water (25 c.c.), and 10N-hydrochloric acid (2·2 c.c.) were refluxed for one hour. The product, which separated on cooling, was filtered off, dissolved in water and reprecipitated with hydrochloric acid. After being dried, the *dihydrochloride* (4787) was crystallised from alcohol; colourless needles, m. p. 259—261° (yield, 11·2 g.) (Found in material dried at 100° : C, 47·4; H, 6·5; N, 13·0; Cl′, 13·3. $C_{22}H_{28}N_5Br,2HCl,2H_2O$ requires C, 47·9; H, 6·2; N, 12·7; Cl′, 12·9%).

4-(6′-*Bromo-β-naphthylamino*)-2-γ-*dibutylaminopropylamino*-6-*methylpyrimidine* (XIII; R=$[CH_2]_3{\cdot}NBu^{\alpha}_2$).—4-Chloro-2-γ-dibutylaminopropylamino-6-methylpyrimidine (7·8 g.) and 6-bromo-β-naphthylamine (5·5 g.) were added to water (25 c.c.) containing 10N-hydrochloric acid (2·5 c.c.) and the mixture refluxed for one hour. On adding more hydrochloric acid and cooling 4-(6′-*bromo-β-naphthylamino*)-2-γ-*dibutylaminopropylamino*-6-*methylpyrimidine dihydrochloride* (4788) separated and was filtered off. It was purified by dissolving in water, reprecipitaing with hydrochloric acid and crystallising the dried product from alcohol–ethyl acetate; it was thus obtained as colourless needles, m. p. 250—252° (yield, 8·8 g.) (Found : C, 51·6; H, 6·7; N, 11·4; Cl′, 11·7. $C_{26}H_{36}N_5Br,2HCl,2H_2O$ requires C, 51·4; H, 6·9; N, 11·5; Cl′, 11·7%).

4-(6′-*Bromo-β-naphthylamino*)-2-δ-*diethylamino-α-methylbutylamino*-6-*methylpyrimidine* (XIII; R=$CHMe{\cdot}[CH_2]_3{\cdot}NEt_2$).—4-Chloro-2-δ-diethylamino-α-methylbutylamino-6-methylpyrimidine (9·5 g.), 6-bromo-β-naphthylamine (7·4 g.), water (50 c.c.), and 10N-hydrochloric acid (3·3 c.c.) were refluxed for 2 hours. The resulting clear solution was cooled, made alkaline with sodium hydroxide, and extracted with chloroform. The chloroform extract was shaken with 5% acetic acid, and the acetic acid extract separated and added to excess sodium hydroxide. The precipitated oil was extracted with chloroform, and the solution dried (K_2CO_3) and evaporated. The oil was characterised as its *dipicrate*, which separated from β-ethoxyethanol as yellow prisms, m. p. 240—242° (Found : C, 46·6; H, 4·3; N, 16·4. $C_{24}H_{33}N_5Br,2C_6H_3O_7N_3$ requires C, 46·6; H, 4·1; N, 16·6%). The *dihydrochloride* (5063), prepared by evaporating to dryness under reduced pressure a solution of the base in 2N-hydrochloric acid, crystallised from alcohol–ethyl acetate as colourless laminæ, m. p. 260—262° (Found : C, 53·4; H, 6·3; N, 12·5; Cl′, 12·5. $C_{24}H_{32}N_5Br,2HCl$ requires C, 53·0; H, 6·3; N, 12·9; Cl′, 13·1%).

4-(6′-*Bromo-β-naphthylamino*)-2-γ-*piperidinopropylamino*-6-*methylpyrimidine* (XIII; R = $[CH_2]_3{\cdot}N{<}CH_2]_4{>}CH_2$).—A mixture of 4-chloro-2-γ-piperidinopropylamino-6-methylpyrimidine (5·4 g.), 6-bromo-β-naphthylamine (4·45 g.), water (40 c.c.), and 10N-hydrochloric acid (2 c.c.) was refluxed for 1 hour. From the clear solution the product began to separate after about 10 minutes. After adding more hydrochloric acid to make the mixture acid to Congo red and cooling, the product was filtered off, dried, and crystallised from alcohol giving the *dihydrochloride* (5041) as colourless elongated prisms, m. p. 288—289° (yield, 10·3 g.) (Found : C, 48·8; H, 6·0; N, 12·2; Cl′, 13·2. $C_{23}H_{28}N_5Br,2HCl,2H_2O$ requires C, 49·0; H, 6·0; N, 12·4; Cl′, 12·6%).

4-(6′-*Bromo-β-naphthylamino*)-2-γ-n-*butylaminopropylamino*-6-*methylpyrimidine* (XIII; R = $[CH_2]_3{\cdot}NHBu^{\alpha}$).—Crude 4-chloro-2-γ-*n*-butylaminopropylamino-6-methylpyrimidine (6·4 g.), 6-bromo-β-naphthylamine (5·5 g.), water (25 c.c.), and 10N-hydrochloric acid (2·5 c.c.) were refluxed for 2 hours, and the solution cooled and made alkaline with sodium hydroxide. The liberated base was extracted with chloroform and this in turn extracted with 5% acetic acid. The acetic acid extract was made alkaline with sodium hydroxide and the base isolated with chloroform. It formed an oil which did not crystallise but was characterised as its *dipicrate*, which separated from β-ethoxyethanol in yellow prisms, m. p. 219—220° (Found : C, 45·3; H, 4·1; N, 16·9. $C_{22}H_{28}N_5Br,2C_6H_3O_7N_3$ requires C, 45·3; H, 3·6; N, 17·1%). The *dihydrochloride* (5152), prepared by dissolving the base in warm 2N-hydrochloric acid and cooling, was filtered off and dried. It crystallised from alcohol as colourless prisms, m. p. 301—303° (Found : C, 50·8; H, 5·6; N, 13·9; Cl′, 12·8. $C_{22}H_{28}N_5Br,2HCl$ requires C, 51·3; H, 5·8; N, 13·6; Cl′, 13·8%).

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[*Received, July 31st,* 1945.]