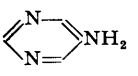
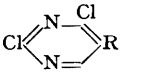
354. *A New Synthesis and the Chemical Properties of 5-Aminopyrimidine.*

By N. WHITTAKER.

[*With Physical Measurements* by T. S. G. JONES.]

Suitable conditions have been determined for the catalytic dechlorination of chloropyrimidines. 5-Aminopyrimidine (I) has been synthesised from uracil, *via* 5-amino-2 : 4-dichloropyrimidine (II; R = NH_2), in 44% over-all yield. The chemical and some physical properties of the former have been examined and a number of derivatives prepared. 5-Aminopyrimidine did not give a diazonium salt, but its dichloro-derivative was converted by nitrous acid into diazouracil (VII); the mechanism of this reaction is discussed.

DURING a recent study of derivatives of heterocyclic amines a quantity of 5-aminopyrimidine (I) was required. This substance had been synthesised by Roblin, Winnek, and English (*J. Amer. Chem. Soc.*, 1942, **64**, 567) from nitromalonic aldehyde by a five-stage process developed from the earlier work of Hale and Brill (*J. Amer. Chem. Soc.*, 1912, **34**, 82). For the preparation of 5-aminopyrimidine in quantity a simpler synthesis seemed desirable, and accordingly possible alternative routes were examined, one of which proved to be satisfactory.

(I.)   (II.)

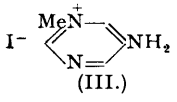
Uracil (2 : 4-dihydroxypyrimidine) was nitrated by a modification of Johnson's method (*J. Amer. Chem. Soc.*, 1919, **41**, 783) and the 5-nitrouracil thus produced was converted into 2 : 4-dichloro-5-nitropyrimidine (II; R = NO_2) in good yield (cf. Isay, *Ber.*, 1906, **39**, 252) by boiling phosphoryl chloride in the presence of dimethylaniline. The catalytic influence of dimethylaniline on the replacement of hydroxyl by chlorine in hydroxypyrimidines, which obviates the use of sealed tubes, has already been well exemplified (Kenner, Lythgoe, Todd, and Topham, *J.*, 1943, 575; Baddiley and Topham, *J.*, 1944, 678; King, King, and Spensley, *J.*, 1947, 1247), but examples are encountered where the method is not satisfactory. It was not possible to convert 5-nitrobarbituric acid into the corresponding trichloronitropyrimidine, but this might be the consequence of further reaction of the chloropyrimidine with the dimethylaniline (cf. Ross, *J.*, 1948, 1129; King *et al.*, *loc. cit.*). The chlorination of uracil by this method gave 2 : 4-dichloropyrimidine in excellent yield.

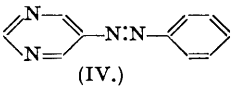
Ferrous hydroxide reduced 2 : 4-dichloro-5-nitropyrimidine (II; R = NO_2) to 5-amino-2 : 4-dichloropyrimidine (II; R = NH_2) in good yield. Before attempting the dechlorination of this substance experiments were first conducted with 2 : 4 : 6-trichloro- and 2 : 4-dichloropyrimidine. Aqueous-alcoholic suspensions of 2 : 4 : 6-trichloropyrimidine containing a palladium–charcoal catalyst were shaken with hydrogen at atmospheric pressure in the presence of various bases as hydrogen chloride acceptors. When the base was sodium carbonate some hydrolysis of reactive chlorine occurred and a low uptake of hydrogen was recorded. In the presence of sodium acetate, which gave a buffered solution of slightly acid pH, reduction of the pyrimidine ring occurred in addition to dechlorination with absorption of more than 5 mols. of hydrogen. With magnesium oxide, however, the theoretical uptake of 3 mols. was achieved. Similarly with 2 : 4-dichloropyrimidine in the presence of magnesium oxide, reaction ceased when 2 mols. of hydrogen had been absorbed, and pyrimidine was isolated, by precipitation as the mercuric chloride compound, in 92% yield. When this procedure was applied to 5-amino-2 : 4-dichloropyrimidine (II; R = NH_2), preferably in aqueous suspension, a magnesium chloride compound of 5-aminopyrimidine, and thence 5-aminopyrimidine, were isolated in good yield.

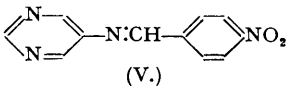
In an attempt to effect simultaneous reduction of the nitro-group and dechlorination of 2 : 4-dichloro-5-nitropyrimidine (II; R = NO_2) with palladium–charcoal and hydrogen under pressure, a colourless solution was obtained which did not contain 5-aminopyrimidine (cf. the similar finding by Roblin *et al.*, *loc. cit.*, with 2-chloro-5-nitropyrimidine). This solution was oxidised in the air to a water-soluble azo-product. The reduction of 2 : 4-dichloro-5-nitropyrimidine (II; R = NO_2) with zinc dust by the method used for the corresponding 6-methyl

compound (Gabriel and Colman, *Ber.*, 1901, **34**, 1250—1252) did not produce 5-amino-2-chloropyrimidine. 5-Amino-2 : 4-dimercaptopyrimidine, prepared from 2 : 4-dichloro-5-nitropyrimidine (II; R = NO_2) by reaction with sodium hydrogen sulphide, was heated under reflux in alkaline solution with a large excess of Raney nickel (Mozingo *et al.*, *J. Amer. Chem. Soc.*, 1943, **65**, 1013), but no 5-aminopyrimidine was isolated.

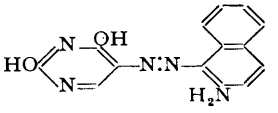
5-Aminopyrimidine formed colourless prisms, m. p. 171—172° (Roblin *et al.*, *loc. cit.*, give m. p. 170—171°). Molecular-weight determinations confirmed the mononuclear structure, so that the high melting point, and the low solubility in non-polar solvents, must be attributed to a strengthening of the crystal lattice by hydrogen-bonding between the amino-groups and the negatively charged ring-nitrogen atoms of adjacent molecules. 5-Aminopyrimidine is stable in the solid state or in aqueous solution, but the addition of mineral acid causes ready atmospheric oxidation with formation of dark amorphous material. The substance has only weak basic character, giving in concentrated aqueous solution a neutral (litmus) reaction, consistent with the pK_a value of 2·6 given in a later section. 5-Aminopyrimidine readily formed a methiodide (III) by reaction with cold methanolic methyl iodide. Bromine in aqueous solution converted 5-aminopyrimidine into an intractable black substance, and therefore further characterisation was sought by the preparation of derivatives with substituents on the amino-group rather

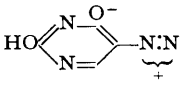

(III.)


(IV.)


(V.)

(VI.)



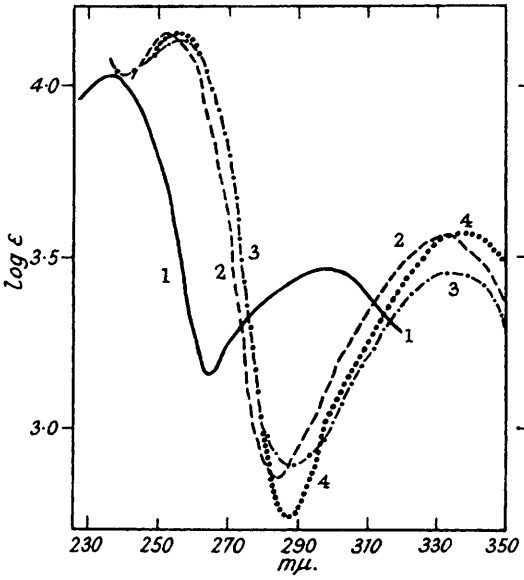

(VII.)

than by electrophilic substitution in the nucleus. 5-Acetamido- and 5-benzamido-pyrimidine were obtained by customary methods. The inherent low nucleophilic reactivity of the functional group of 5-aminopyrimidine was observed in the absence of reaction with nitrosobenzene under conditions which produce azobenzene from aniline and nitrosobenzene (Baeyer, *Ber.*, 1874, **7**, 1638). When the components were heated in acetic acid, however, 5-phenylazopyrimidine (IV) was obtained. Similarly, vigorous conditions were necessary to produce the Schiff's base 5-*p*-nitrobenzylideneaminopyrimidine (V). 5-Aminopyrimidine did not give a diazonium salt with nitrous acid or nitrosylsulphuric acid. In contrast, 5-amino-2 : 4-dichloropyrimidine (II; R = NH_2) formed a diazonium salt which could be coupled with β-naphthylamine in acid solution to give an azo-compound in the form of a purple hydrochloride. The new red base was shown to be 2-amino-1-(2 : 4-dihydroxy-5-pyrimidylazo)naphthalene (VI) by reduction with sodium dithionite to 1 : 2-diaminonaphthalene, which gave the characteristic 2 : 3-diphenyl-5 : 6-benzoquinoxaline with benzil. The possibility that the reagents used in the neutralisation of the purple hydrochloride had effected hydrolysis of some reactive chlorine in the pyrimidine nucleus was excluded by the fact that hot aqueous 2-hydroxyethylamine produced the same azo-compound (VI) and not a 2-hydroxyethylamino-derivative. In the reaction of 5-amino-2 : 4-dichloropyrimidine (II; R = NH_2) with nitrous acid, hydrolysis of both chlorine atoms had occurred simultaneously with diazotisation, and thus it was possible to effect diazotisation by using 0·5 molecular equivalent of hydrochloric acid per mole of sodium nitrite. The solution produced in this way had a characteristic instability to heat, but by neutralisation of the hydrochloric acid formed by hydrolysis, the known heat-stable diazouracil (VII) was produced (Behrend and Ernert, *Annalen*, 1890, **258**, 347; Johnson, Baudisch, and Hoffmann, *Ber.*, 1931, **64**, 2629; Bogert and Davidson, *Proc. Nat. Acad. Sci.*, 1932, **18**, 215). The representation (VII) is arbitrary since the precise structure of diazouracil has not yet been determined. It is now suggested that in acid solution an equilibrium exists between the dihydroxypyrimidinediazonium chloride and diazouracil, although strongly on the side of the latter; the former is the unstable compound which undergoes coupling. It is postulated that a combination of two factors is responsible for the production of a diazo-compound from 5-amino-2 : 4-dichloropyrimidine (II; R = NH_2) which are not operative with 5-aminopyrimidine: at the instant of reaction with nitrous acid the chlorine atoms of the transitional diazonium salt, activated by the exocyclic positive pole, are replaced by hydroxyl and rapid transformation into the stabilised zwitterion structure of diazouracil follows. If this explanation is correct the ability to form diazo-compounds may well be confined to those 5-aminopyrimidines with at

least one hydroxyl substituent, or a substituent capable of conversion into hydroxyl, *e.g.*, alkylthio- or alkoxy-, under the conditions of diazotisation.

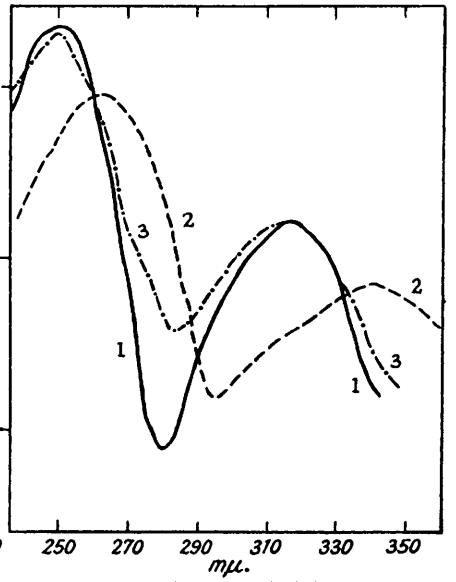
Physical Measurements.—Ultra-violet absorption spectra. Fig. 1 shows the ultra-violet absorption curves for 5-aminopyrimidine in solution in water and 0·1N-hydrochloric acid. The two peaks found in the former solvent are also present in the acid solution but both are shifted to longer wave-lengths, and the intensity of absorption is increased. Cation formation must therefore involve the attachment of a proton to one of the equivalent ring-nitrogen atoms rather than to the amino-group, since by Waterman's rule the spectrum of the 5-pyrimidyl-

FIG. 1.



5-Aminopyrimidine (I) : —— *in water*, – – – – *in* 0·1N-HCl. *5-Amino-1-methylpyrimidinium iodide* (III) : . . . . *in water*, – · – · – *in* 0·1N-HCl.

FIG. 2.



5-Amino-2 : 4-dichloropyrimidine (II; R = NH_2) : —— *in water*, – – – – *in* 5N-HCl, – · – · – *in* 5N-HCl *subsequently neutralised by sodium acetate.*

ammonium ion should approximate to that of pyrimidine itself ($\lambda_{max.}$ 245 mμ.; $\varepsilon_{max.}$ = 3000; Heyroth and Loofbourow, *J. Amer. Chem. Soc.*, 1934, **56**, 1728). This interpretation is confirmed by the absorption curves of 5-aminopyrimidine methiodide (Fig. 1), the structure of which is known from its method of formation and chemical properties. The great similarity of the curves for this compound in acid and neutral solution with that of 5-aminopyrimidine in acid solution is evident. A small correction should be made for the absorption of the iodide ion in the region of 250 mμ., but would not significantly affect the course of the curves much above 260 mμ. 5-Aminopyrimidine is rapidly decomposed in 5N-hydrochloric acid. The band at

Name.	Medium.	λ (mμ.).	ε (max.).	λ (mμ.).	ε (max.).
5-Aminopyrimidine	Water	236	11,000	298	3,100
	0·1N-HCl	253	14,400	332	3,700
5-Amino-1-methylpyrimidinium iodide	Water	256	14,300	337	3,700
	0·1N-HCl	257	14,000	339	3,100
5-Amino-2 : 4-dichloropyrimidine	Water	250	15,100	316	4,100
	5N-HCl	265	9,700	340	2,700
	5N-HCl neutralised by sodium acetate	251	14,300	317	4,000
5-Benzamidopyrimidine	Water	256	17,500	—	—
	0·1N-HCl	262	20,900	—	—
	5N-HCl	265	26,400	—	—
5-Acetamidopyrimidine	Water	236	13,000	275 (inflexion)	2,800
5-Phenylazopyrimidine	10% EtOH in water	232	9,500	315	15,400
5-*p*-Nitrobenzylideneaminopyrimidine	EtOH	303	20,400	—	—

~250 mμ. is scarcely affected but that at ~330 mμ. progressively decreases in intensity and broadens.

5-Amino-2 : 4-dichloropyrimidine also takes up a proton on a ring-nitrogen atom in acid solution to give a spectrum with a corresponding shift in wave-length but a diminution in intensity, and differing from that of 2 : 4-dichloropyrimidine (Heyroth and Loofbourow, *loc. cit.*). In 5N-hydrochloric acid (Fig. 2) this compound is more stable than 5-aminopyrimidine, for, on its neutralisation with sodium acetate, the spectrum reverts to that of the neutral solution, although with a distinct change in the minimum.

Details for these and other compounds are collected in the Table.

Ionisation constant. The apparent dissociation constants of the conjugate acid of 5-aminopyrimidine in water at 25° and 40° have been found potentiometrically (the glass electrode being used in a cell with a liquid junction) to be 2·60 ± 0·01 and 2·62 ± 0·03 respectively (Roblin, cited by Albert, Goldacre, and Phillips, *J.*, 1948, 2246, found 2·83).

Experimental.

5-Nitrouracil.—Uracil was prepared in 92% yield from commercially available 2-thiouracil by Wheeler and Liddle's method (*Amer. Chem. J.*, 1908, **40**, 547). The initially exothermic nitration with fuming nitric acid (Johnson, *loc. cit.*) should be conducted at 60—65° with external cooling, before the final evaporation in an open dish. On a 150—200 g. scale the yield of 5-nitro-compound was 97—98%.

2 : 4-*Dichloro-5-nitropyrimidine* (II; R = NO_2).—5-Nitrouracil (26 g.), phosphoryl chloride (redistilled; 130 ml.), and dimethylaniline (redistilled; 32 ml.) were heated, with occasional shaking, until reaction commenced. When this had subsided the mixture was refluxed for 70 minutes, then cooled, and most of the phosphoryl chloride evaporated off under reduced pressure. The residue was poured on ice with vigorous stirring and, after 5 minutes, extracted with ether (500 ml.); the extract was washed with water and dried (Na_2SO_4). Removal of the ether and distillation of the residue gave 2 : 4-dichloro-5-nitropyrimidine which, when redistilled, was a pale yellow oil (23·0 g., 72%), b. p. 138—139°/14 mm., m. p. 29—30°. With larger preparations the yield was reduced, *e.g.*, from 214 g. of 5-nitrouracil the yield was 161 g. (61%).

Delay in extracting the product with ether reduced the yield; in an experiment with 16 hours' delay none of the product was obtained.

2 : 4-*Dichloropyrimidine.*—Uracil (50 g.), phosphoryl chloride (250 ml.), and dimethylaniline (62 ml.), refluxed for 2 hours and worked up as above, gave 2 : 4-dichloropyrimidine (57·6 g., 87%), m. p. 61—62°, b. p. 100°/22 mm.

5-*Amino*-2 : 4-*dichloropyrimidine* (II; R = NH_2).—To a suspension of ferrous hydroxide (from ferrous sulphate heptahydrate, 516 g., and barium hydroxide octahydrate, 586 g., in hot water, 6 l.) at 70—75°, molten 2 : 4-dichloro-5-nitropyrimidine (40 g.) was added with powerful stirring, and the temperature quickly raised to 90—95°. Reduction was rapid, and, after 30 minutes' heating, the mixture was filtered hot and the black residue washed with hot water. The aqueous liquors were concentrated *in vacuo* to *ca.* 1·5 l., the crystalline product was collected, and the mother-liquor extracted with chloroform (2 × 400 ml.). After being dried (Na_2SO_4) the extract was evaporated, and the combined product sublimed (110—115°/2 mm.) to give colourless dense prisms, which were recrystallised from benzene–light petroleum (80—100°). 5-*Amino*-2 : 4-*dichloropyrimidine* (27·6 g., 82%) was thus obtained in colourless needles, m. p. 121·5—122·5° (Found: C, 29·55; H, 2·0; N, 25·55; Cl, 42·75. $C_4H_3N_3Cl_2$ requires C, 29·3; H, 1·85; N, 25·6; Cl, 43·3%).

Catalytic Dechlorination of Chloropyrimidines.—The volumes quoted below are at N.T.P. A palladium–charcoal catalyst (*ca.* 3% of Pd) was used throughout, 1 g. requiring 30 ml. hydrogen for saturation.

(*a*) A mixture of 2 : 4 : 6-trichloropyrimidine 2 g.) (Baddiley and Topham, *loc. cit.*), magnesium oxide (2 g.), catalyst (0·5 g.), alcohol (20 ml.), and water (60 ml.) was shaken with hydrogen at one atmosphere. Absorption ceased after 190 minutes when 765 ml. of hydrogen had been utilised (2nd expt., 783 ml.; calc., 747 ml.).

(*b*) When 2 : 4-dichloropyrimidine (15 g.), magnesium oxide (15 g.), catalyst (4 g.), alcohol (75 ml.), and water (150 ml.) were treated as in (*a*), absorption of hydrogen (4710 ml.; calc., 4635 ml.) was complete after 155 minutes. The mixture was then filtered, the residue was washed with water, and the combined filtrates were steam-distilled until the distillate gave no further precipitate with aqueous mercuric chloride. The total distillate was treated with an excess of mercuric chloride solution; pyrimidine mercurichloride ($C_4H_4N_2,HgCl_2$) was thus obtained (32·4 g., 92%).

(*c*) A mixture of 5-amino-2 : 4-dichloropyrimidine (6 g.), magnesium oxide (6 g.), catalyst (6 g.), and water (150 ml.) absorbed 1940 ml. hydrogen during 190 minutes (calc., 1820 ml.). After filtration the residue was washed with water, and the combined filtrates were evaporated to dryness *in vacuo*. The magnesium chloride compound of 5-aminopyrimidine thus left was dried, and then dissolved in warm alcohol (150 ml.) and poured through a column of activated alumina (200 g.). The column was washed with alcohol, and the colourless eluate evaporated to leave a residue of 5-aminopyrimidine, which crystallised from benzene, forming first colourless needles but later prisms (2·66 g., 77%), m. p. 171—172° with sublimation [Found: C, 50·95; H, 4·7; N, 44·05; *M* (Rast; camphor), 90, 110. Calc. for $C_4H_5N_3$: C, 50·55; H, 5·25; N, 44·2%; *M*, 95].

When the dechlorination was effected in 50% aqueous alcohol a further 30 minutes was required, but in alcoholic solution reaction was incomplete after 5 hours.

5-Amino-2 : 4-dimercaptopyrimidine.—To a solution of sodium hydrogen sulphide, prepared by saturating a solution of sodium (5 g.) in alcohol (100 ml.) and water (30 ml.) at room temperature with hydrogen sulphide, a solution of 2 : 4-dichloro-5-nitropyrimidine (5 g.) in alcohol (15 ml.) was added dropwise with shaking. The mixture was refluxed for 2 hours, cooled, diluted with water, and acidified with acetic acid. When the solvent had been evaporated *in vacuo*, the residue was suspended in water (500 ml.), and sufficient sodium carbonate solution added to dissolve the product. Sulphur was removed by filtration and the filtrate acidified with acetic acid to precipitate *5-amino-2 : 4-dimercaptopyrimidine* (3·5 g.). This substance dissolved in hot water to give a pale yellow solution from which brown needles, yellow in transmitted light, separated on cooling, but it was unstable to prolonged heating with water. It darkened above 220° and decomposed at *ca.* 270° with evolution of hydrogen sulphide (Found : C, 31·1; H, 2·9; N, 26·2; S, 40·25. $C_4H_5N_3S_2$ requires C, 30·2; H, 3·15; N, 26·4; S, 40·25%).

5-Amino-1-methylpyrimidinium Iodide (III).—A solution of 5-aminopyrimidine (0·5 g.) in methanol (5 ml.) was treated with methyl iodide (1 ml.) and after 72 hours the crystalline product (0·64 g.) was collected (m. p. 166—167°) (mother-liquors yielded a further 0·29 g.) and recrystallised from alcohol. The *methiodide* was obtained as prisms, yellow-brown in reflected light and pale yellow in transmitted light, m. p. 166—167°. A powdered specimen was colourless (Found : C, 25·75; H, 3·5; N, 17·55; I, 53·7. $C_5H_8N_3I$ requires C, 25·3; H, 3·4; N, 17·7; I, 53·6%). The product dissolved readily in water to give a neutral (litmus) solution.

5-Acetamidopyrimidine.—5-Aminopyrimidine (0·25 g.), acetic anhydride (1 ml.), and benzene (5 ml.) were refluxed for 2 hours. On cooling, *5-acetamidopyrimidine* separated as colourless prisms, m. p. 147—149°, raised by recrystallisation from benzene to 148—149° (Found : C, 53·1; H, 5·0; N, 31·15. $C_6H_7ON_3$ requires C, 52·55; H, 5·1; N, 30·65%).

5-Benzamidopyrimidine.—Benzoyl chloride (3·3 ml.) was added to a solution of 5-aminopyrimidine (2 g.) in dry pyridine (20 ml.) and the reaction liquid left overnight. The pyridine was evaporated *in vacuo* and the residue shaken with chloroform (*ca.* 200 ml.) and water (50 ml.). The chloroform layer was separated, washed once with water, and evaporated. The residual solid was purified by recrystallisation from water (some dark residue), and then from benzene, to give *5-benzamidopyrimidine* as colourless prisms (2·5 g.), m. p. 146—147° (Found : C, 66·55; H, 4·5; N, 21·3. $C_{11}H_9ON_3$ requires C, 66·35; H, 4·5; N, 21·1%).

5-Phenylazopyrimidine (IV).—A mixture of 5-aminopyrimidine (0·5 g.), nitrosobenzene (0·6 g.), and glacial acetic acid (6 ml.) was refluxed for 2½ hours. The solvent was evaporated *in vacuo* and the dark residue digested with hot water and evaporated once more. A chloroform extract of the residue was washed with water, dried (Na_2SO_4), and chromatographed (Al_2O_3), the column being developed with chloroform. A diffuse yellow-orange band descended the column to yield an orange eluate, from which the chloroform was evaporated, and the residual material purified by further chromatography (Al_2O_3) in benzene and then by recrystallisation from light petroleum (b. p. 60—80°). *5-Phenylazopyrimidine* was thus obtained as red plates (0·1 g.), m. p. 97·5—98° (Found : C, 65·3; H, 4·45; N, 30·05. $C_{10}H_8N_4$ requires C, 65·2; H, 4·35; N, 30·45%); it was sparingly soluble in hot water, from which fine orange needles separated on cooling.

5-p-*Nitrobenzylideneaminopyrimidine* (V) was the product of heating 5-aminopyrimidine (50 mg.), *p*-nitrobenzaldehyde (75 mg.), and glacial acetic acid (0·1 ml.) at 160° for 5 minutes. After cooling, the solid product was ground under water and collected (110 mg.), m. p. 185—186°. By recrystallisation from alcohol the sparingly soluble product was obtained in fine yellow needles, unchanged in m. p. (Found : C, 57·7; H, 3·35; N, 24·7. $C_{11}H_8O_2N_4$ requires C, 57·9; H, 3·5; N, 24·55%).

Reactions with Nitrous Acid.—(a) *5-Aminopyrimidine.* To an ice-cooled solution of 5-aminopyrimidine (0·25 g.), in water (6 ml.) and concentrated hydrochloric acid (0·8 ml.), under carbon dioxide, a solution of sodium nitrite (0·19 g.) in water (2 ml.) was added drop-wise. Vigorous evolution of gas occurred immediately. After 5 minutes the liberated gases were swept by a current of carbon dioxide through a U-tube containing ferrous sulphate-impregnated pumice, and the nitrogen collected in a nitrometer over 50% aqueous potassium hydroxide. The volume of nitrogen collected (45·4 ml.; 45·2 ml. at N.T.P.) corresponded to 77% conversion of amino-group into nitrogen. The same reaction at −5° gave 43·4 ml. nitrogen.

(b) *5-Amino-2 : 4-dichloropyrimidine* (II; R = NH_2). A solution of 5-amino-2 : 4-dichloropyrimidine (1 g., 1 mol.) in hot water (15 ml.) was cooled quickly to 0°, and 10N-hydrochloric acid (2 ml., 3·3 mols.) added to the suspension of fine needles thus produced. A cold solution of sodium nitrite (0·41 g., 1 mol.) in water (4 ml.) was then added quickly with shaking and cooling. After 2 minutes the nitrous acid-free, clear solution was poured into a solution prepared by heating β-naphthylamine (1 g.), water (40 ml.), and 10N-hydrochloric acid (1 ml.) and rapid cooling to 0°. The mixture was shaken at 0° for 1 hour, and the purple crystalline precipitate collected, and washed with 0·1N-hydrochloric acid and then with water. This substance was heated for a few minutes with dilute aqueous sodium hydroxide or sodium acetate containing 10% of alcohol, acidified with acetic acid, and cooled. The red solid (0·98 g.), m. p. 264—265° (decomp.), was purified by chromatography (Al_2O_3) in pyridine, the product being eluted with pyridine–methanol–water. The solvent was evaporated from the eluate, and the residual solid digested with aqueous acetic acid and cooled. Recrystallised from 2-ethoxyethanol it gave red plates and prisms of *2-amino-1-(2 : 4-dihydroxy-5-pyrimidylazo)naphthalene* (VI), m. p. 269—270° (decomp.) (Found : C, 59·55; H, 3·9; N, 25·0. $C_{14}H_{11}O_2N_5$ requires C, 59·8; H, 3·9; N, 24·9%). Crude (VI) (1·95 g.) was suspended in hot aqueous sodium hydroxide and reduced with sodium dithionite. When the solid had dissolved the liquid was filtered, cooled and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated in a stream of nitrogen.

To the residual 1 : 2-diaminonaphthalene thus obtained, benzil (1·45 g.), alcohol (20 ml.), and concentrated hydrochloric acid (0·1 ml.) were added. The mixture was refluxed for 1 hour, cooled, and diluted with water, and the precipitated solid thrice recrystallised from alcohol to give 2 : 3-diphenyl-5 : 6-benzoquinoxaline as straw-coloured prisms (0·9 g.), m. p. 148—149° (Found : C, 86·65; H, 4·9; N, 8·7. Calc. for $C_{24}H_{16}N_2$: C, 86·75; H, 4·8; N, 8·45%). Lawson (*Ber.*, 1885, **18**, 2426) gives m. p. 147°.

When 5-amino-2 : 4-dichloropyrimidine (1 g., 1 mol.) was diazotised in the presence of 0·3 ml. (0·5 mol.) of 10N-hydrochloric acid, a clear solution was also obtained. Evolution of nitrogen was slight at 0°, but with heating this became vigorous and a yellow-brown solid separated. When the acid (1·5 mols.) was neutralised by magnesium oxide or aqueous ammonia the solution was stable to heat, and by concentration *in vacuo* diazouracil was isolated as an amorphous yellow solid. The neutralised solution coupled slowly with β-naphthol (Bogert and Davidson, *loc. cit.*).

Physical Determinations.—Absorption spectra. These were determined photographically, the Hilger Medium Quartz Spectrograph and Spekker Photometer being used. Solutions were made up from weighed quantities of the materials in volumetric flasks.

Ionisation constants. Weighed quantities of 5-aminopyrimidine (0·5 m.-mol., 47·5 mg.) were dissolved in 5·00 ml. of conductivity water and titrated with 1·00M-HCl in a cell containing a glass electrode, calibrated by means of the phthalate, borate, and tetroxalate buffers recommended by Bates, Pinching, and Smith (*J. Res. Nat. Bur. Stand.*, 1950, **45**, 418). The solution was stirred by a current of nitrogen of suitable humidity. The reference electrode was a large calomel half-cell containing 3·5M-KCl and connected by a capillary bridge of 3·5M-KCl. The thermostat was maintained at 40° ± 0·1° or 25° ± 0·1°. Potentials were measured by using an electrometer tetrode as null indicator, the difference in potential of the electrode train and a Tinsley precision potentiometer being applied to the control grid. Potentials were reproducible to 0·1 mv. The titrant was admitted from a micrometer syringe, about thirty small additions being made. The pH values calculated from the potentials were plotted against the volume of titrant to give a smooth curve. The pK_a' values were then calculated from convenient points on the curve according to the equation, $pK_a' = pH - \log\{([B] + [H^+])/([BH^+] - [H^+])\}$, where [B], [BH+], and [H+] are the calculated concentrations of the base, conjugate acid, and hydrogen ion, corrected for the dilution caused by addition of acid but not for the activity coefficients.

The author is indebted to Mr. A. Bennett for microanalyses, and to Mr. W. D. Chiswell for technical assistance.

CHEMICAL DIVISION, WELLCOME RESEARCH LABORATORIES,
BECKENHAM, KENT.

[*Received, February 3rd*, 1951.]