460. *Hydropyrimidines. Part III.*[1] *Reduction of Aminopyrimidines.*

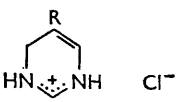
By R. F. Evans.

2-Amino- and 2-acylamino-pyrimidines have been catalytically reduced in acidic media to the 1,4,5,6-tetrahydro-derivatives. Under similar conditions, 4- and 5-aminopyrimidines underwent hydrogenolysis, accompanied by ammonia formation. However 5-acetamidopyrimidine was satisfactorily reduced to the tetrahydro-derivative. The basic and spectral properties of the reduced derivatives are discussed.

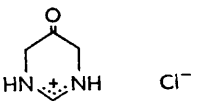
Previous Parts [1,2] described the preparation of alkyl- and aryl-substituted 1,4,5,6-tetrahydropyrimidines. The reduction of the aminopyrimidines has now been investigated. In acidic media, 2-aminopyrimidine, its 4,6-dimethyl derivative, and its acyl derivatives, absorbed two moles of hydrogen over palladised charcoal. The product was shown to be the 1,4,5,6-tetrahydro-derivative by alkaline hydrolysis to the trimethylenediamine. The free base was liberated from 2-amino-1,4,5,6-tetrahydropyrimidine hydrochloride by sodium ethoxide. In contrast to the parent 1,4,5,6-tetrahydropyrimidine, which rapidly hydrolysed in aqueous solution at room temperature,[2] the ring in the 2-amino-compound was broken only in boiling water; the attack of the hydrolytic agent on C-2 was evidently hindered by the combined steric and electronic effects of the amino-group.

4-Aminopyrimidine was reduced very slowly in acid, in the presence of palladised charcoal. The product was unstable, and only degradation fragments were isolated or detected. These were an ammonium salt, formaldehyde, and an amidinium chloroplatinate. The evidence favoured initial formation of a 1,2,5,6-tetrahydro-derivative in preference to the 1,4,5,6-isomer.[3] No reduction was observed, under a variety of conditions, with the 2-, 5-, and 6-amino-, 6-methyl, and 2,6-dimethyl derivatives of 4-aminopyrimidine, some as free bases, others as salts. 4-Aminopyrimidine was substantially unaffected by ethereal lithium aluminium hydride.

5-Aminopyrimidine, its 2,4-dichloro-derivative, and 5-nitro-2,4-dichloropyrimidine, all gave the same products when reduced with hydrogen and palladised charcoal, namely ammonium chloride and 1,4,5,6-tetrahydro-5,5-dihydroxypyrimidine hydrochloride. 5-Aminopyrimidine absorbed one mole of hydrogen during reduction, so that the initial product must be a dihydro-compound of structure (I; R = NH_2). Hydrolysis of such an



(I)



(II)

enamine would readily occur to give the substance (I; R = OH). Hydration of the keto-group in the tautomer (II) of this substance is facilitated [4] by the inductive effect ($-I$) of the positive charge on the amidinium system. The *gem*-diol thus formed readily gave

[1] Part II, Brown and Evans, *J.*, 1962, 4039.
[2] Brown and Evans, *J.*, 1962, 527.
[3] Aft and Christensen, *J. Org. Chem.*, 1962, **27**, 2170.
[4] Lyle, Adel, and Lyle, *J. Org. Chem.*, 1959, **24**, 342.

ketonic derivatives (oxime, phenylhydrazone, 2,4-dinitrophenylhydrazone), and the infrared spectrum confirmed the absence of a free keto-group.

5-Acetamidopyrimidine gave the 1,4,5,6-tetrahydro-derivative on catalytic reduction in aqueous acid. The acetyl group of the reduced product was rapidly lost in hot aqueous acid, and the 5-amino-1,4,5,6-tetrahydropyrimidine dihydrochloride so formed could, in turn, be hydrolysed in alkali to 1,2,3-triaminopropane.

Ionisation.—1,4,5,6-Tetrahydropyrimidine and its 2-amino-derivative are highly basic molecules (pK_a 13·0 and 14·1, respectively [1,2]) as befits their amidine structures. The introduction of two hydroxy-groups into the 5-position of the 1,4,5,6-tetrahydropyrimidine molecule, *i.e.*, at a distance of two carbon atoms from the basic centre, lowered the pK_a by 3 units. This was greater than when the hydroxy-groups were on different carbon atoms [the pK_a of di-(2-hydroxyethyl)amine,[5] for example, is smaller than that of diethylamine [6] by 2·09 units]. Acylation of 2-amino-1,4,5,6-tetrahydropyrimidine, as with guanidine,[7] brought about a large decrease (6—7 units) in the pK_a value [1] (14·1). Benzoylation of 2-aminopyrimidine caused a much smaller drop (2 units) in the pK_a value [7] (3·54), comparable with that observed with other 2-amino-heterocycles.[7,8] 2-Benzamidopyrimidine (pK_a 11·20) was a stronger acid than benzamide [9] (pK_a 13—14), because of the electron-attracting properties of the pyrimidine ring.

Infrared Spectra.—A selection of bands in the infrared spectra of 1,4,5,6-tetrahydropyrimidines are listed in Table 1. The intense band due to asymmetric $(N{:::}C{:::}N)^+$

TABLE 1.

Infrared spectra (cm.$^{-1}$) of substituted 1,4,5,6-tetrahydropyrimidine salts.

Subst.	Acid in salt	$\nu N{:::}\overset{+}{C}{:::}N$	Double-bond stretching region	ν(NH) Amidine	ν(NH) Amide	ν(OH)
2-NH_2		1679 *		3200		
	HCl	1677		3240, 3340, 3100		
2-NH·COMe	$MeCO_2H$		1663, 1680	2500	3280	
	HCl		1623, 1680, 1715	3205, 2870	3285	
	$HHgCl_3$		1623, 1710, 1690	3285		
2-NH·CO·Ph	HCl		1626, 1694, 1680	3120	3270	
2-NH_2–4,6-Me_2	HCl	1665	1630	3060, 3200, 3330		
	HHg_2Cl_5	1660	1628	3350		
5-NH_2	2HCl	1690		3000, 3155		
	Hg_2Cl_6	1690		3285		
5-NH·CO·Me	HCl,H_2O		1658, 1690	3180, 3360	3260	3490
5,5-$(OH)_2$	HCl	1696		3205		3350
5=NOH	HCl	1700	1656	3100, 3210		3386

* ν(as N–C–N).

stretching is prominent in the 1650—1700 cm.$^{-1}$ region and varies slightly with the anion in the molecule. The diminution in hydrogen bonding accompanying the change of anion from hydrochloride to chloromercurate is reflected in the N–H stretching region, where several broad bands are replaced by one sharp peak. The presence of an amide group in some of the compounds made band assignments uncertain in the double-bond stretching region; these bands are listed separately in order of diminishing intensity. The intense band at 1696 cm.$^{-1}$ in the spectrum of the 5,5-dihydroxy-compound is to be regarded as a ν [as $(N{:::}C{:::}N)^+$] vibration rather than as the carbonyl stretching of a ketone. It is rather too low for the carbonyl stretching frequency of a ketonic group in a six-membered ring [10a] containing charged nitrogen.[10b] Conversion of the compound into the oxime does

[5] Bower, Robinson, and Bates, *J. Res. Nat. Bur. Stand.*, 1962, **66**, *A*, 71.
[6] A. G. Evans and Hamann, *Trans. Faraday Soc.*, 1951, **47**, 34.
[7] Albert, Goldacre, and Phillips, *J.*, 1948, 2240.
[8] Jones and Katritzky, *J.*, 1959, 1317.
[9] Branch and Clayton, *J. Amer. Chem. Soc.*, 1928, **50**, 1680.
[10] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1960, (*a*) p. 147; (*b*) p. 98; (*c*) p. 268.

not cause this band to disappear, but moves it to a slightly higher frequency, whilst a new band, due to C=N stretching, appears in the expected region.[10c]

Experimental

Analyses are by Dr. J. E. Fildes and her staff. Substances were examined chromatographically on Whatman paper No. 1 (method A), or No. 4 (method B), in butanol–5N-acetic acid (7 : 3 v/v) by the ascending technique. Papers were viewed under a mercury lamp emitting radiation of 254 mμ; compounds which did not absorb in the ultraviolet region were rendered visible by exposure to iodine vapour. Light petroleum had b. p. 60—80°, and "catalyst" refers to 10% palladised charcoal.[11] Ammonium halides were identified from infrared spectra.

General Method of Reduction.—The pyrimidine derivative, in a suitable solvent, was shaken with hydrogen and catalyst at room temperature until hydrogen uptake ceased (Table 2). The

Table 2.

Experimental conditions for reductions (at room temperature).

Pyrimidine derivative	Wt. (g.)	Tetrahydro-product	Wt. of catalyst (g.)	Solvent and vol. (ml.)	Time (hr.)
2-Amino	5	1,4,5,6-	1	2N-HCl (80)	4
,, ...	1	,,	0·5	Glacial acetic acid (10)	2·5
2-Amino-4,6-dimethyl	1·23	,,	0·3	0·5N-HCl (20)	15
2-Acetamido	0·63	,,	0·31	0·1N-HCl (45·65)	2·75
,, ...	1	,,	0·5	Glacial acetic acid (10)	2·3
,, ...	0·79	,,	0·4	Acetic anhydride (10) (at 100°)	1
2-Benzamido	0·5	,,	0·2	0·25N-HCl (10)	7
4-Amino	4·7	1,2,5,6-	1	2N-HCl (50)	13
5-Amino	0·9	5,5-Dihydroxy-1,4,5,6-	0·5	0·8N-HCl (26)	6
5-Amino-2,4-dichloro	10·4	,,	2·5	Water (40)	8·5
5-Nitro-2,4-dichloro ...	5	,,	1	Water (20)	18
5-Acetamido	3·21	1,4,5,6-	1·6	0·1N-HCl (234)	4

mixture was filtered and the filtrate evaporated at 100°/20 mm. (25°/20 mm. for the 5-amino-series). The residue (80—100%) was crystallised from a suitable solvent.

Reduction of 2-Aminopyrimidine Derivatives.—(*a*) 2-Aminopyrimidine gave 2-amino-1,4,5,6-tetrahydropyrimidine hydrochloride, m. p. 148—153° (lit.,[1] 152—157°) (from propan-1-ol–ethyl acetate), identified from R_F value (method A) and as the picrate and pentachlorodimercurate.[1,12] No dihydrochloride [13] was obtained when an ethanolic solution was saturated with hydrogen chloride. The hydrochloride (5·1 g.) in ethanol (10 ml.) was mixed with a solution from sodium (0·82 g.) and ethanol (10 ml.). Removal of sodium chloride, and of volatile constituents at 20°/0·2 mm., and distillation of the residue, afforded 2-*amino*-1,4,5,6-*tetrahydropyrimidine*, m. p. 81—85°, b. p. 140—150°/0·2 mm. (Found: C, 48·6; H, 8·9; N, 41·7. $C_4H_9N_3$ requires C, 48·5; H, 9·15; N, 42·4%).

Reduction of 2-aminopyrimidine in glacial acetic acid afforded deliquescent 2-*amino*-1,4,5,6-*tetrahydropyrimidine acetate*, m. p. 140—145° (from propan-2-ol–light petroleum) (Found: C, 45·0; H, 8·5; N, 26·0. $C_6H_{13}N_3O_2$ requires C, 45·3; H, 8·2; N, 26·4%), identified by conversion into the picrate.

(*b*) Reduction of 2-amino-4,6-dimethylpyrimidine ultimately afforded 2-*amino*-1,4,5,6-*tetrahydro*-4,6-*dimethylpyrimidine hydrochloride monohydrate*, m. p. 66—68° (from propan-2-ol–light petroleum) (Found: C, 39·8; H, 8·6; N, 23·0. $C_6H_{14}ClN_3,H_2O$ requires C, 39·7; H, 8·9; N, 23·1%). This lost water *in vacuo* over phosphorus pentoxide at room temperature, giving the *anhydrous compound*, m. p. 114—115° (Found: C, 44·1; H, 8·8; Cl, 21·7; N, 25·6. $C_6H_{14}ClN_3$ requires C, 44·0; H, 8·6; Cl, 21·7; N, 25·7%). The *trichloromercurate* formed needles, m. p. 135·5—137° (from propan-2-ol) (Found: C, 16·6; H, 3·2; N, 9·7. $C_6H_{14}Cl_3HgN_2$

[11] *Org. Synth.*, Coll. Vol. III, 687.
[12] Evans, *J.*, 1962, 4259.
[13] Smith and Christensen, *J. Org. Chem.*, 1955, **20**, 829.

requires C, 16·6; H, 3·2; N, 9·7%). The *picrate* had m. p. 183—184° (from methanol) (Found: C, 40·3; H, 4·5; N, 23·6. $C_{12}H_{16}N_6O_7$ requires C, 40·4; H, 4·5; N, 23·6%).

(*c*) In 0·1N-hydrochloric acid, 2-acetamidopyrimidine [14] was reduced to *2-acetamido-1,4,5,6-tetrahydropyrimidine hydrochloride*, m. p. 218—221° (from ethanol) (Found: C, 41·2; H, 6·6; Cl, 19·5; N, 23·4. $C_6H_{12}ClN_3O$ requires C, 40·6; H, 6·8; Cl, 20·0; N, 23·7%). The *picrate* had m. p. 196—200° (from methanol) (Found: C, 38·9; H, 3·6; N, 23·0. $C_{12}H_{11}N_6O_8$ requires C, 38·9; H, 3·8; N, 22·7%). The *trichloromercurate* had m. p. 135—136° (from ethanol) (Found: C, 16·0; H, 2·7; Cl, 23·5; N, 9·2. $C_6H_{12}Cl_3HgN_3$ requires C, 16·05; H, 2·7; Cl, 23·7; N, 9·4%). The *acetate*, obtained by direct reduction in glacial acetic acid or acetic anhydride, had m. p. 72—75° (from propan-2-ol–light petroleum) (Found: C, 48·0; H, 7·8; N, 20·9. $C_8H_{15}N_3O_3$ requires C, 47·8; H, 7·5; N, 20·9%), and could be converted into the picrate.

2-Benzamido-1,4,5,6-tetrahydropyrimidine Hydrochloride.—A mixture of 2-amino-1,4,5,6-tetrahydropyrimidine (0·4 g.) and benzoyl chloride (0·57 g.) in dry pyridine (15 ml.) was set aside for 2 hr. and evaporated at 20°/0·15 mm. Extraction of the residue with hot benzene and evaporation of the extract at 20°/0·15 mm. furnished the *hydrochloride*, m. p. 207—211° (from acetone) (Found: C, 54·8; H, 5·5; N, 17·5. $C_{11}H_{14}ClN_3O$ requires C, 55·1; H, 5·9; N, 17·5%). An identical product (m. p., mixed m. p., and infrared spectrum) was obtained from the reduction of 2-benzamidopyrimidine, prepared by the reaction of 2-aminopyrimidine with benzoyl chloride in pyridine,[15] in preference to the use of Schotten–Baumann conditions, or of 2-aminopyrimidine with phenyl benzoate.[16]

Hydrolyses.—(*a*) 2-Amino-1,4,5,6-tetrahydropyrimidine (1 g.) and water (10 ml.) were boiled for ¾ hr., filtered, and mixed with picric acid (3 g.) in ethanol (10 ml.). The mixture was evaporated at 100°/20 mm. and the residue extracted with boiling benzene (3 × 20 ml.). The insoluble fraction was repeatedly crystallised from ethanol, and separated into trimethylenediamine picrate [m. p. and mixed m. p. 248—250° (decomp.)] and *3-ureidopropylamine picrate*, m. p. 167—171° (Found: C, 34·7; H, 4·0; N, 23·9. $C_{10}H_{14}N_6O_8$ requires C, 34·7; H, 4·0; N, 24·3%). 2-Amino-1,4,5,6-tetrahydropyrimidine was recovered as the picrate from a solution of its hydrochloride (6 g.) and potassium hydroxide (10 g.) in water (20 ml.) after ½ hr. at 0° and 1½ hr. at 20°.

(*b*) 2-Amino-1,4,5,6-tetrahydro-4,6-dimethylpyrimidine hydrochloride (0·36 g.) and sodium hydroxide (0·5 g.) in water (10 ml.) were refluxed for 2 hr. Ammonia was evolved, and the mixture was evaporated at 100°/0·1 mm. The distillate, after titration with dilute nitric acid to a Methyl Red end-point, was evaporated at 100°/20 mm. Two crystallisations of the residue from ethanol afforded β-DL-2,4-diaminopentane dinitrate, m. p. 198—199·5° (decomp.) (lit.,[17] 195°) (Found: C, 26·2; H, 7·0; N, 24·3. Calc. for $C_5H_{16}N_4O_6$: C, 26·3; H, 7·0; N, 24·55%).

(*c*) Hydrolysis of 2-acetamido-1,4,5,6-tetrahydropyrimidine acetate, as in (*b*), afforded trimethylenediamine, isolated and identified as the dihydrochloride (infrared spectrum).

Reduction of 4-Aminopyrimidine Derivatives.—(*a*) 4-Aminopyrimidine gave an oil which did not contain starting material (paper chromatography, methods A and B). Successive crystallisations from methanol–ethanol and methanol afforded ammonium chloride. The mother-liquor furnished *acrylamidinium tetrachloroplatinate*, m. p. >310° (from water) (Found: C, 15·6; H, 2·6; Cl, 29·3; N, 11·4; Pt, 39·75. $C_6H_{14}Cl_4N_4Pt$ requires C, 15·0; H, 2·95; Cl, 29·6; N, 11·7; Pt, 40·7%). The infrared spectrum (KCl disc) had $\nu_{max.}$ 3140 (NH) and 1671 cm.$^{-1}$ [as $(N{=}{=}C{=}{=}N)^+$].

Reduction of 4-aminopyrimidine hydrobromide afforded a solution which, on evaporation at 30°/20 mm., gave a distillate containing formaldehyde (chromotropic acid test [18]). Ammonium bromide was isolated from the residue.

No reduction was observed when a methanolic solution of the amino-compound was refluxed with Raney nickel [19] under nitrogen for 30 min., or heated with Raney nickel and hydrogen at 75°/30 atm. for 2 hr. Only starting material was recovered when 4-aminopyrimidine was refluxed with ethereal lithium aluminium hydride.

No reduction occurred when aqueous solutions of the monohydrochlorides of the 2,4-, 4,5-,

[14] Brown and Short, *J.*, 1953, **331**.
[15] Whittaker, *J.*, 1951, 1565.
[16] Takatori and Ueda, *J. Pharm. Soc. Japan*, 1951, **71**, 1373.
[17] Dippel, *Rec. Trav. chim.*, 1931, **50**, 525.
[18] West and Sen, *Z. analyt. Chem.*, 1956, **153**, 177.
[19] Fox and von Praag, *J. Amer. Chem. Soc.*, 1960, **82**, 486.

and 4,6-diamino-, 4-amino-6-methyl-, and 4-amino-2,6-dimethyl-pyrimidines were separately shaken with catalyst and hydrogen under atmospheric pressure at 20 or at 100°. *4,5-Diaminopyrimidine monohydrochloride* had m. p. 241—244° (from ethanol) (Found: C, 32·9; H, 4·8; N, 38·0. $C_4H_7ClN_4$ requires C, 32·8; H, 4·8; N, 38·2%), and the *dihydrochloride* had m. p. 231° (from aqueous ethanol containing hydrochloric acid) (Found: C, 26·2; H, 4·2; N, 30·3. $C_4H_8Cl_2N_4$ requires C, 26·25; H, 4·4; N, 30·6%). 4-Amino-6-methylpyrimidine was not reduced in propan-1-ol by 5% rhodium on alumina and hydrogen at 100°/50 atm. for 7 hr.

Reduction of 5-Aminopyrimidine Derivatives.—(*a*) 5-Amino-2,4-dichloropyrimidine was prepared from 5-nitrouracil by the method of Whittaker.[15] Reaction with acetic anhydride in boiling benzene afforded the *5-acetamido-compound*, m. p. 129—133° (from acetone–light petroleum) (Found: C, 35·0; H, 2·3; Cl, 33·9; N, 20·45. $C_6H_5Cl_2N_3O$ requires C, 35·0; H, 2·45; Cl, 34·4; N, 20·4%). Reduction of the amino-compound afforded a residue which was extracted with hot propan-2-ol (8 × 25 ml.). The extracts deposited solids which were combined, and crystallised repeatedly from aqueous propan-2-ol, to give *1,4,5,6-tetrahydro-5,5-dihydroxypyrimidine hydrochloride* (0·76 g., 8%), m. p. 210—220° (decomp.) (Found: C, 31·3; H, 6·0; Cl, 23·35; N, 18·1. $C_4H_9ClN_2O_2$ requires C, 31·5; H, 5·95; Cl, 23·2; N, 18·4%). The *gem*-dihydroxy-compound was converted into a *phenylhydrazone*, m. p. 168—170° (decomp.) (from methanol) (Found: C, 53·3; H, 6·0; Cl, 16·0; N, 25·3. $C_{10}H_{13}ClN_4$ requires C, 53·45; H, 5·8; Cl, 15·8; N, 24·9%), a *2,4-dinitrophenylhydrazone*, m. p. 203° (decomp.) (from methanol–ethanol–light petroleum) (Found: C, 38·3; H, 3·7; Cl, 10·9; N, 26·0. $C_{10}H_{11}ClN_6O_4$ requires C, 38·2; H, 3·5; Cl, 11·3; N, 26·7%), and an *oxime*, m. p. 171° (decomp.) (from ethanol–light petroleum) (Found: C, 32·2; H, 5·5; Cl, 23·9; N, 27·5. $C_4H_8ClN_3O$ requires C, 32·1; H, 5·4; Cl, 23·7; N, 28·1%). Ammonium chloride was isolated from the solid sparingly soluble in propan-2-ol by fractional crystallisation from methanol–ethanol–acetone. The *gem*-dihydroxy-compound and ammonium chloride were also isolated from the reduction of 5-aminopyrimidine and of 2,4-dichloro-5-nitropyrimidine.

(*b*) Reduction of 5-acetamidopyrimidine gave a *monohydrate* (from aqueous propan-2-ol) (Found: C, 36·7; H, 7·1; N, 21·8. $C_6H_{12}ClN_3O,H_2O$ requires C, 36·85; H, 7·2; N, 21·5%) which lost water between 90 and 100° to give anhydrous *5-acetamido-1,4,5,6-tetrahydropyrimidine hydrochloride*, m. p. 245—248° (decomp.) (Found: C, 40·4; H, 6·8; Cl, 20·05; N, 23·65. $C_6H_{12}ClN_3O$ requires C, 40·6; H, 6·8; Cl, 20·0; N, 23·7%).

5-Amino-1,4,5,6-tetrahydropyrimidine Dihydrochloride.—5-Acetamido-1,4,5,6-tetrahydropyrimidine hydrochloride (2·43 g.) and 0·5N-hydrochloride acid (50 ml.) were refluxed for 2 hr. and evaporated at 100°/20 mm. Repeated crystallisation of the residue (2·6 g.) from aqueous ethanol afforded the *dihydrochloride*, m. p. 327° (decomp.) (Found: C, 27·8; H, 6·5; Cl, 41·3; N, 24·2. $C_4H_{11}Cl_2N_3$ requires C, 27·9; H, 6·4; Cl, 41·2; N, 24·4%). The *bistrichloromercurate* had m. p. 256—262° (decomp.) (from aqueous ethanol) (Found: C, 6·5; H, 1·4; N, 5·9. $C_4H_{11}Cl_6Hg_2N_3$ requires C, 6·7; H, 1·55; N, 5·9%). The picrate formed yellow needles, m. p. 252—262° (decomp.) (from aqueous ethanol) (Found: C, 34·1; H, 3·0; N, 22·9. $C_{16}H_{15}N_9O_{14}$ requires C, 34·5; H, 2·7; N, 22·6%).

Hydrolysis of 5-Amino-1,4,5,6-tetrahydropyrimidine Dihydrochloride.—The amino-compound (0·34 g.) in N-sodium hydroxide (10 ml.) was refluxed for 1 hr. and evaporated at 100°/0·1 mm. The distillate was acidified with hydrochloric acid and evaporated. The residue, after two crystallisations from aqueous ethanol, gave 1,2,3-triaminopropane trihydrochloride, m. p. 247° (decomp.) [lit.,[20] 250° (decomp.)] (Found, for a sample dried at 60°/20 mm.: C, 18·2; H, 6·9; Cl, 53·05; N, 21·3. Calc. for $C_{13}H_{14}Cl_3N_3$: C, 18·15; H, 7·1; Cl, 53·6; N, 21·2%).

pK_a *Determination.*—Ionisation constants at 20° were determined potentiometrically or spectrophotometrically[8] with an Optika CF4 instrument.[21] The values obtained for the 1,4,5,6-tetrahydropyrimidines were: 2-acetamido 8·34 ± 0·01; 2-benzamido[8] 7·12 ± 0·02; 5-amino $pK_{a1} > 12$ and pK_{a2} 5·89 ± 0·01, 5,5-dihydroxy 10·03 ± 0·05. 2-Benzamidopyrimidine[8] had acidic pK_a 11·20 ± 0·05 and basic pK_a 1·56 ± 0·04.

Spectra.—Ultraviolet spectra were determined with a Perkin-Elmer Spectracord model 4000-A double-beam spectrophotometer or with a Shimadzu recording spectrophotometer model RS27 and the maxima checked with a Hilger Uvispek Mark V manual instrument. Infrared spectra were taken with a Perkin-Elmer 21 double-beam spectrophotometer fitted

[20] Curtius and Hesse, *J. prakt. Chem.*, 1900, [2], **62**, 241.
[21] Albert and Serjeant, "Ionization Constants," Methuen, London, 1962.

with a sodium chloride prism. The compounds were examined in potassium bromide discs, except for the chloroplatinates which were examined in potassium chloride discs.

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