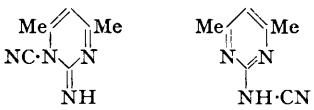
356. *2-Cyanoamino-4 : 6-dimethylpyrimidine and Complexes formed by Pyrimidines with Urea and Related Compounds.*

By S. BIRTWELL.

2-Cyanoamino-4 : 6-dimethylpyrimidine, previously designated 1-cyano-1 : 2-dihydro-2-imino-4 : 6-dimethylpyrimidine, gives on acid hydrolysis first 4 : 6-dimethyl-2-ureidopyrimidine and then a 1 : 1 molecular complex of 2-hydroxy-4 : 6-dimethylpyrimidine and urea. This complex was incorrectly formulated by earlier workers. Molecular complexes are also formed between a number of other pyrimidines and urea. Compounds related to urea such as cyanoguanidine, biuret, and thiourea may replace urea in these complexes, whose structures are discussed.

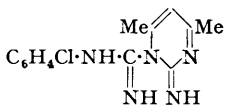
The reactions between arylamines and 2-cyanoamino- and 2-ureido-4 : 6-dimethylpyrimidine are described.

To the product of reaction between acetylacetone and cyanoguanidine, Hale and Vibrans (*J. Amer. Chem. Soc.*, 1918, **40**, 1060) assigned structure (I). Nevertheless, in an attempt to prepare compound (III) by addition of *p*-chloroaniline (as its hydrochloride) to (I), 2-*p*-chlorophenylguanidino-4 : 6-dimethylpyrimidine (IV) (Cliffe, Curd, Rose, and Scott, *J.*, 1948, 574) was isolated as sole product. It appears, therefore, that the correct structure is 2-cyanoamino-4 : 6-dimethylpyrimidine (II), and this has been confirmed by an unambiguous synthesis from 2-chloro-4 : 6-dimethylpyrimidine and sodium cyanamide. The condensation of cyanoguanidine with a β-diketone, therefore, is similar to its reactions with β-keto-esters (Pohl, *J. pr. Chem.*, 1908, **77**, 533; Crowther, Curd, and Rose, *J.*, 1948, 586) and malonic ester (Merck, D.R.-P. 158,591) which also give 2-cyanoaminopyrimidines.



(I)

(II)



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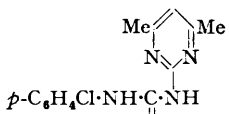
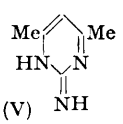


(IV)

Several attempts to prepare (I) by reaction of 2-amino-4 : 6-dimethylpyrimidine (VI) with bromine and potassium cyanide or with cyanogen bromide were unsuccessful.

The crux of the argument advanced by Hale and Vibrans (*loc. cit.*) in support of structure (I) lay in the formation, on dilute acid hydrolysis, of 1 : 2-dihydro-2-imino-4 : 6-dimethylpyrimidine (V) (as its monohydrate), which, it was claimed, was different from the 2-amino-4 : 6-dimethylpyrimidine (VI) of A. and C. Combes (*Bull. Soc. chim.*, 1892, **7**, 788). Such a theory is untenable now, so the product of hydrolysis of (I) has been re-examined; it has been shown to be a 1 : 1 complex of 2-hydroxy-4 : 6-dimethylpyrimidine and urea, being readily obtained by mere crystallisation of equimolecular proportions of urea and the pyrimidine from alcohol; it was first prepared by Evans (*J. pr. Chem.*, 1892, **46**, 352; 1893, **48**, 489) and A. and C. Combes (*Bull. Soc. chim.*, 1893, **7**, 791) from acetylacetone and excess of urea. These authors, who called the substance "diurimidoacetylacetone," suggested that it was 2 : 4-biscarbamyliminopentane (VII), whereas de Haan (*Rec. Trav. chim.*, 1908, **27**, 162) and Hale (*J. Amer. Chem. Soc.*, 1914, **36**, 104) regarded it as 1 : 2 : 3 : 4-tetrahydro-4 : 6-dimethyl-4-ureido-2-pyrimidone (VIII). Nevertheless, de Haan's observations (*loc. cit.*), and the identity between the ultra-violet absorption spectrum of this substance and the curve obtained by superimposing the spectrum of 2-hydroxy-4 : 6-dimethylpyrimidine on that of urea, suggest that it is a molecular complex. This has been confirmed by conversion into the sodium salt of 2-hydroxy-4 : 6-dimethylpyrimidine, and into dixanthylurea. Boarland and McOmie (*J.*, 1952, 3722) have recently shown that the sulphur analogue of (VII) ("dithiourimidoacetylacetone") is also, in fact, a molecular complex of thiourea and 2-mercapto-4 : 6-dimethylpyrimidine.

4 : 6-Dimethyl-2-ureidopyrimidine is readily obtained from (II) by the action of cold concentrated sulphuric acid, or boiling dilute sulphuric acid (2 min.). The same compound may be synthesised in small yield from (VI) by reaction with urethane [cf. Bamberger (*Ber.*, 1887, **20**, 69) for a similar preparation of guanylurea]. 4 : 6-Dimethyl-2-ureidopyrimidine gives the molecular complex described above when boiled for 1 hr. with dilute sulphuric acid. By fusing it with *p*-chloroaniline hydrochloride or sulphanilamide hydrochloride at 150—160°, one obtains the 2-*p*-chlorophenylureido- or the 2-*p*-sulphamylphenylureido-derivative, respectively. The free amines are much less satisfactory for this purpose.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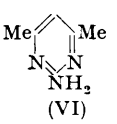
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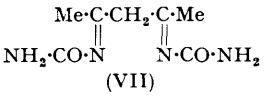
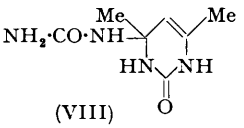

(VII)


(VIII)

The reaction between (II) and 2 mols. of sulphanilamide at 170° has been described as giving 4 : 6-dimethyl-2-sulphanilamidopyrimidine and sulphanilylguanidine (B.P. 635,876). Despite numerous attempts it has not been possible to substantiate this result. However, equimolecular proportions of sulphanilamide hydrochloride and (II) combine at 78° in alcohol to give *N*-2-(4 : 6-dimethylpyrimidyl)-*N'*-*p*-sulphamylphenylguanidine, whereas sulphanilamide itself when dissolved with (II) in either boiling alcohol or water gives a 1 : 1 complex. It may be conclusively demonstrated that this substance *is* a complex by diazotisation and coupling to give *p*-sulphamylphenylazo-β-naphthol and by comparison of its ultra-violet absorption spectrum with those of sulphanilamide and (II) determined separately. The curves are additive, and isosbestic points are shown at 212, 261, and 290 mμ (in water).

Arising out of this investigation, a number of pyrimidines were examined for the property of complex formation with urea, and urea-like compounds. Among the complexes observed was that between urea and 2-amino-4 : 6-dimethylpyrimidine, and those of thiourea with 2-amino- and 2-mercapto-4 : 6-dimethylpyrimidine which have since been reported (Bray, Lake, and Thorpe, *Biochem. J.*, 1951, **48**, 400; Boarland and McOmie, *loc. cit.*). These examples and the urea–2-hydroxy-4 : 6-dimethylpyrimidine complex described above are particular cases of a phenomenon which is now shown to be quite general for these chemical types.

Our results, which are illustrative rather than exhaustive, are set out in Tables 1, 2, and 3.

TABLE 1. *Equimolecular complexes of some dimethylpyrimidines and urea.**

Dimethyl-pyrimidine	Solvent	M. p.†	Formula	Analytical data Found, % C	H	N	Reqd., % C	H	N	Notes ‡
2-Hydroxy-4 : 6-	98% EtOH	203° †	$C_6H_8ON_2,CH_4ON_2$	46·1	6·5	30·2	45·7	6·5	30·4	A
2-Amino-4 : 6- ...	,,	192—193 †	$C_6H_9N_3,CH_4ON_2$	45·9	7·1	38·0	46·0	7·1	38·2	A
2-Mercapto-4 : 6-	95% ,,	199—200 †	$C_6H_8N_2S,CH_4ON_2$	42·1	6·2	27·8	42·0	6·0	28·0	A
4-Hydroxy-2 : 6-	98% ,,	160—162	$C_6H_8ON_2,CH_4ON_2$	46·1	6·6	29·8	45·7	6·5	30·4	B
4-Amino-2 : 6- ...	,, ,,	153—155	$C_6H_9N_3,CH_4ON_2$	46·0	7·4	38·0	46·0	7·1	38·2	B, C

* The constituents were mixed in equimolar proportion in solution.
† M. p.s designated thus are with decomp.
‡ A. Composition and m. p. unchanged on recrystallisation.
B. Not recrystallised.
C. Complex rather soluble in EtOH, so crystallisation induced by concentration.

The following pyrimidines, in alcoholic solution, failed to give complexes with urea : 2 : 4 : 6-trimethyl-, 4-ethoxy-2 : 6-dimethyl-, 4 : 6-dimethyl-2-sulphanilamido-, 4 : 6-dimethoxy-2-sulphanilamido-. 4-Methyl*iso*cytosine crystallised with some urea, but not in stoicheiometric proportion. Benzamide did not give a complex when substituted for urea.

The 1 : 1 complexes shown in Table 1 were the most easily prepared, being generally of low solubility in alcohol, of high m. p., and stable to recrystallisation. In these respects

the complexes with 4-hydroxy- and with 4-amino-2 : 6-dimethylpyrimidine were less stable than with the isomeric 2-hydroxy- and 2-amino-compounds.

The complexes in Table 2 crystallised with urea in molecular ratios other than unity. 2-Cyanoamino- and 2-ureido-4 : 6-dimethylpyrimidine formed crystalline complexes only from solutions containing excess of urea and gave the pure (less soluble) pyrimidine itself on recrystallisation. The complex with 4-methyluracil crystallised from aqueous alcohol containing excess of urea only very slowly during several days. On the other hand, excess of the pyrimidine was used in the cases of the more soluble 2-ethoxy- and 2-methylthio-pyrimidines. It is also noteworthy that different solvents may lead to complexes of different molecular ratio.

TABLE 2. *Complexes of dimethylpyrimidines and urea in other than equimolecular ratio.*

4 : 6-Dimethyl-pyrimidine	Solvent	Molar ratio, urea : pyrimidine in soln.	M. p.*	Found, % C	H	N	Formula	Reqd., % C	H	N	Notes †
2-Cyano-amino-	MeOH	7 : 1	184—185°	43·4	6·0	41·1	$2C_7H_8N_4,3CH_4ON_2$	42·7	5·9	41·0	A
2-Ureido-	,,	11 : 2	188—189	38·2	6·4	38·6	$C_7H_{10}ON_4,2CH_4ON_2$	37·8	6·3	39·1	B
2-Ethoxy-	98% EtOH	1 : 1	134—136	40·1	7·5	33·8	$C_8H_{12}ON_2,3CH_4ON_2$	39·8	7·2	33·7	C
2-Ethoxy-	MeOH	1 : 4	134—135	43·3	7·1	31·2	$C_8H_{12}ON_2,2CH_4ON_2$	44·1	7·3	30·9	D
2-Methylthio-	,,	10 : 3	147—148	39·7	6·7	30·9	$C_7H_{10}SN_2,2CH_4ON_2$	39·4	6·6	30·6	E
(4-Methyl-uracil)	80% Aq. EtOH	10 : 1	301	42·2	4·6	28·0	$2C_5H_6O_2N_2,CH_4ON_2$	42·3	5·1	27·0	F

* All substances showed shrinkage before melting, except the last, which melted with decomp.
† A. After two recrystallisations from methanol, the original pyrimidine was obtained, m. p. and mixed m. p. 234—235°.
B. The complex not recrystallised.
C. M. p. and analysis refer to material after recrystallisation from absolute alcohol, in which it was rather soluble.
D. A very small volume of solvent was used. The complex was not recrystallised.
E. Sufficient methanol was used to obtain complete solution at the boil. The complex was not recrystallised.
F. The complex crystallised very slowly (several days) in low yield.

TABLE 3. *Equimolecular complexes of 2-hydroxy-4 : 6-dimethylpyrimidine with compounds related to urea.**

Urea-like compound	M. p.	Found, % C	H	N	Formula	Reqd., % C	H	N	Notes †
Cyanoguanidine	220—222°	42·5	6·6	38·1	$C_6H_8ON_2,C_2H_3N_4,H_2O$	42·5	6·2	37·2	A, B
Biuret	219—221	42·4	5·9	32·5	$C_6H_8ON_2,C_2H_5O_2N_3$	42·3	5·7	30·8	B
Thiourea	203—204	41·4	6·5	28·4	$C_6H_8ON_2,CH_4N_2S$	42·0	6·0	28·0	B

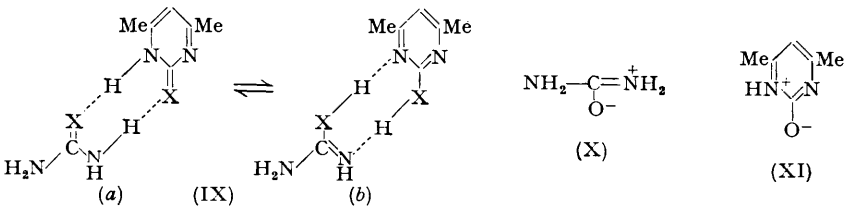
* Equimolar proportions, dissolved in 95% EtOH, were mixed.
† A. Complex obtained as monohydrate. B. Complexes were not recrystallised.

In Table 3 are listed the complexes between 2-hydroxy-4 : 6-dimethylpyrimidine and urea-like substances. They closely resemble the 1 : 1 complexes formed by urea.

Although any discussion of the structure of these complexes can only be very speculative, it is probable that the compounds are associated by hydrogen bonding both in the crystal and in solution. This association may be especially powerful owing to cyclic structures being involved; *e.g.*, the complexes of Table 1 may well be represented by (IX, *a* and *b*; X = O, S, NH).

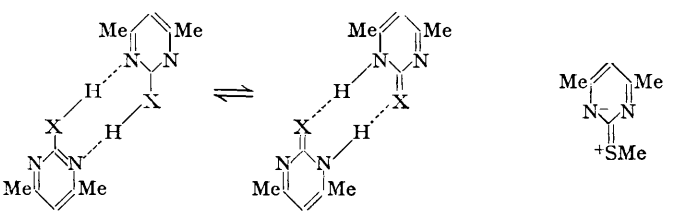
In urea, and the pyrimidines of Table 1, bipolar mesomeric forms such as (X) and (XI) may be expected to make large contributions to their respective structures, and would greatly favour hydrogen-bond formation (which is regarded as largely electrostatic in character : see Symposium on the Hydrogen Bond, Royal Institute of Chemistry, 1949). It is necessary to point out, however, that Marshall and Walker (*J.*, 1951, 1004), on the

basis of the observed similarity in the spectra of 2-hydroxy-4 : 6-dimethylpyrimidine (which exists in the dihydro-keto-form) and its cation, concluded that the canonical form (XI) makes little contribution to the structure. In this, however, they failed to take into account that an equilibrium will exist in solution between the tautomeric hydroxy- and dihydro-keto-forms, a point which has been stressed by Brown and Short (*J.*, 1953, 331). It is the author's opinion, also, that pyrimidines of this type constitute a further example of mesohydric tautomerism (Hunter, *J.*, 1945, 806), protonic resonance occurring in such associated structures as (XII, *a* and *b*)—hence the impossibility of isolating the different tautomeric forms. Equilibrium between the two structures would be attained almost instantaneously and ultra-violet absorption spectra would reveal only the predominating, more stable one.



(*a*) (IX) (*b*) (X) (XI)

Some of the pyrimidines in Table 2 may receive important contributions to their structure from canonical forms similar to (XI). In others, a bipolar mesomeric structure such as (XIII) has been postulated (Boarland and McOmie, *loc. cit.*) and might be held equally to favour complex formation, although of a different type.



(*a*) (XII) (*b*) (XIII)

Ionic forms can make only slight contributions to the structures of 2 : 4 : 6-trimethylpyrimidine and to 4-ethoxy-2 : 6-dimethylpyrimidine, and this may be the reason for their failure to form complexes. A similar explanation may serve for the inability of benzamide to replace urea. On the other hand, some pyrimidines whose structures must receive large contributions from bipolar forms have not given complexes, and one can only conclude that the many requirements for crystal formation over and above mere intermolecular association are not fulfilled in these cases.

Experimental

M. p.s are uncorrected.

2-Cyanoamino-4 : 6-dimethylpyrimidine (II).—(*a*) Prepared by the method of Hale and Vibrans (*loc. cit.*) from cyanoguanidine (80 g.), acetylacetone (134 g.), and 2N-sodium hydroxide (40 c.c.) in water (1 l.), at 95—100°, this *pyrimidine* (contrast structure assigned by Hale and Vibrans, *loc. cit.*) was obtained as a white powder (54 g.; m. p. 230—231°) which crystallised from ethanol in small, cream-coloured prisms, m. p. 231—232° after darkening (Found: C, 56·8; H, 5·0; N, 37·7. $C_7H_8N_4$ requires C, 56·8; H, 5·4; N, 37·8%).

(*b*) 2-Chloro-4 : 6-dimethylpyrimidine (28·5 g.) and monosodium cyanamide (13·0 g.) in sodium-dried ethanol (600 c.c.) were heated under reflux with stirring for 20 hr., whereupon sodium chloride separated gradually. A little water was added and carbon dioxide was passed through the cooled solution for 1 hr. Insoluble material was filtered off, and the filtrate was evaporated under reduced pressure, leaving a semi-solid residue, a portion of which dissolved on treatment with acetone (50 c.c.). The crystalline solid which remained was filtered off,

stirred with water, and acidified (faint reaction to Congo-red) with dilute hydrochloric acid. 2-Cyanoamino-4 : 6-dimethylpyrimidine (II) was precipitated and crystallised from methanol, being obtained as almost colourless needles (1·5 g.), m. p. 233—234°, not depressed on admixture with material prepared by method (*a*).

Reactions of 2-*Cyanoamino*-4 : 6-*dimethylpyrimidine with Amines.*—(a) *With* p-*chloroaniline hydrochloride.* *p*-Chloroaniline hydrochloride (4·1 g.) and (II) (3·3 g.) were heated under reflux in ethanol for 4 hr. After being cooled and clarified, the solution was treated with 2N-sodium hydroxide (20 c.c.); 2-*p*-chlorophenylguanidino-4 : 6-dimethylpyrimidine (IV) (5·0 g.) crystallised, and was collected, washed with aqueous methanol, and dried at 60—70°. It had m. p. 206—207°, not depressed by admixture with material prepared from *p*-chlorophenyldiguanide and acetylacetone (Cliffe, Curd, Rose, and Scott, *loc. cit.*).

(b) *With sulphanilamide hydrochloride.* In a similar manner (II) (3·3 g.) and sulphanilamide hydrochloride (5·0 g.) in alcohol (50 c.c.) were heated under reflux for 7½ hr. 4 : 6-*Dimethyl*-2-p-*sulphamylphenylguanidinopyrimidine* (4·0 g.), m. p. 203—205°, crystallised on cooling. It was recrystallised from alcohol (carbon), and obtained as colourless prisms, m. p. 235° (decomp.) (Found : C, 49·1; H, 5·2; N, 26·1. $C_{13}H_{16}O_2N_6S$ requires C, 48·7; H, 5·0; N, 26·2%). The hydrochloride was sparingly soluble in cold dilute hydrochloric acid, but dissolved on warming. It was unaffected by nitrous acid.

(c) *With sulphanilamide.* (i) A mixture of (II) (3·0 g.), sulphanilamide (3·5 g.), and alcohol (50 c.c.) was boiled for 3 hr. At no time was a clear solution obtained. After being cooled, the 1 : 1 *complex* of (II) and sulphanilamide was filtered off, washed with alcohol, and dried at 100° (5·0 g.; m. p. 189—191°). It crystallised from water (charcoal) in glistening needles (4·3 g.; m. p. 190—191°, varying with rate of heating) (Found : C, 48·7; H, 5·2; N, 25·8. $C_{13}H_{16}O_2N_6S$ requires C, 48·7; H, 5·0; N, 26·2%), soluble in both dilute acids and dilute caustic alkalis.

A portion was diazotised and coupled with β-naphthol. After being twice recrystallised from nitrobenzene, the product had m. p. 259—261°, and mixed m. p. 259—261° with material similarly prepared from sulphanilamide and β-naphthol (Found : C, 58·4; H, 4·1; N, 12·6. Calc. for $C_{16}H_{13}O_3N_3S$: C, 58·7; H, 4·0; N, 12·8%).

(ii) Sulphanilamide (1·8 g.) was dissolved in boiling water (50 c.c.), and the cyanoaminopyrimidine (II) (1·5 g.) added. Dissolution of this normally sparingly soluble material was instantaneous. The solution was filtered and cooled immediately, wherupon the molecular compound, m. p. 190—191°, crystallised. It was identical with that prepared by method (i) above.

Hydrolysis of 2-*Cyanoamino*-4 : 6-*dimethylpyrimidine* (II).—A solution of the pyrimidine (II) (4·0 g.) in dilute sulphuric acid (conc. acid, 16 c.c.; water, 80 c.c.) was heated under reflux for 3 hr. By continuing according to Hale and Vibrans (*loc. cit.*), a molecular complex of 2-hydroxy-4 : 6-dimethylpyrimidine and urea (Table 1) was obtained, crystallising from absolute alcohol in pale yellow plates, m. p. and mixed m. p. with a specimen prepared from the two components, 203—204° (decomp.) (Loss at 140° during 2½ hr. : 0·4%).

Isolation of Components from Molecular Complex of 2-*Hydroxy*-4 : 6-*dimethylpyrimidine and Urea.*—(*a*) The complex was suspended in warm alcohol, and alcoholic sodium ethoxide added until the solution gave an alkaline reaction on moist Titan-yellow paper. The sodium salt of 2-hydroxy-4 : 6-dimethylpyrimidine separated, and was filtered off and washed well with alcohol. It was again suspended in alcohol and a stream of carbon dioxide was bubbled through the mixture. The gelatinous precipitate of sodium carbonate was filtered off, and the filtrate was concentrated; yellow crystals of 2-hydroxy-4 : 6-dimethylpyrimidine dihydrate crystallised, m. p. and mixed m. p. 196—198°.

(*b*) The complex (0·25 g.) in 50% acetic acid (20 c.c.) was treated in the cold with a solution of xanthhydrol (0·5 g.) in alcohol (12·5 c.c.). A precipitate slowly formed and was filtered off after 1½ hr. It was washed with 50% alcohol, dried at 90—100°, and then had m. p. 278—279° (decomp.), not depressed on admixture with an authentic specimen of dixanthylurea.

4 : 6-*Dimethyl*-2-*ureidopyrimidine.*—(*a*) The pyrimidine (II) (20·0 g.) was added gradually to concentrated sulphuric acid (100 c.c.) at 10—20°, and the mixture stirred at room temperature to complete dissolution of the solid. With good stirring, ice (100 g.) was introduced gradually, the temperature being kept about 30°. When the acid solution was poured into concentrated sodium hydroxide liquor (NaOH, 160 g.; water, 500 c.c.) and cooled below 30° by addition of ice, 4 : 6-dimethyl-2-ureidopyrimidine was precipitated. This was filtered off, washed well with water, dried at 90—100°, and crystallised from alcohol, affording 12 g. (m. p. and mixed m. p. with material prepared from 2-amino-4 : 6-dimethylpyrimidine, 207—208°).

(*b*) The cyanoaminopyrimidine (II) (6·0 g.) was dissolved in 6N-sulphuric acid (150 c.c.), heated to boiling (8 min.), boiled for a further 2 min., and poured into a solution of 4N-sodium hydroxide (180 c.c.) and ice (300 g.), giving 4 : 6-dimethyl-2-ureidopyrimidine (5·4 g.; m. p. 211°).

(*c*) Urethane (10 g.) and 2-amino-4 : 6-dimethylpyrimidine (VI) (5 g.) were heated for 1 hr. at 190—200° with slow distillation of urethane (and ethanol). The resulting mixture was cooled slightly and diluted with aqueous alcohol. An insoluble by-product was filtered off while still warm; 4 : 6-*dimethyl*-2-*ureidopyrimidine* separated from the cooled filtrates. After successive crystallisations from alcohol (twice) and acetone, it had m. p. 209° and was identical with material obtained in the hydrolysis experiments (*a* and *b*, above) (Found : C, 50·5; H, 6·0; N, 33·0. $C_7H_{10}ON_4$ requires C, 50·6; H, 6·0; N, 33·7%).

Hydrolysis of 4 : 6-*dimethyl*-2-*ureidopyrimidine.* A solution of the ureidopyrimidine (2·0 g.) was hydrolysed with sulphuric acid as described for the cyanoamino-compound. The molecular complex of urea and 2-hydroxy-4 : 6-dimethylpyrimidine (0·9 g.; m. p. 203—204°, decomp.) was again obtained.

Reactions of 4 : 6-*Dimethyl*-2-*ureidopyrimidine with Amines.*—4 : 6-*Dimethyl*-2-p-*sulphamylphenylureidopyrimidine.* Sulphanilamide hydrochloride (2·1 g.) and 4 : 6-dimethyl-2-ureidopyrimidine (1·7 g.) were ground together and heated slowly in an oil-bath. At 150° a slightly exothermic reaction occurred, the temperature rose to 165°, and the contents of the tube solidified. After a further 10 min. at 150—160°, the product was cooled and ground. It was then boiled with water acidified with a few drops of hydrochloric acid. The insoluble 4 : 6-*dimethyl*-2-p-*sulphamylphenylureidopyrimidine* was filtered off, washed well, and dried at 100° (2·3 g.; m. p. 260—264°, decomp.). After recrystallisation from 2-ethoxyethanol, it had m. p. 265° (decomp.) (Found : C, 48·9; H, 4·6; N, 22·0. $C_{13}H_{15}O_3N_5S$ requires C, 48·6; H, 4·7; N, 21·8%). The absence of a free amino-group in this material was demonstrated by attempted diazotisation (nitrosylsulphuric acid method) which failed.

2-p-*Chlorophenylureido*-4 : 6-*dimethylpyrimidine.* Similarly, *p*-chloroaniline hydrochloride (1 g.) and 4 : 6-dimethyl-2-ureidopyrimidine (1 g.), ground together and heated to 160° for ½ hr., gave 2-p-*chlorophenylureido*-4 : 6-*dimethylpyrimidine* (1·3 g.), m. p. 206—209°, crystallising from butanol in long, colourless, felted needles, m. p. 211—212° (Found : C, 57·1; H, 4·9; N, 19·6. $C_{13}H_{13}ON_4Cl$ requires C, 56·4; H, 4·7; N, 20·2%).

Equimolecular Complexes of Pyrimidines with Urea (*see Table* 1).—A solution of the pyrimidine (0·01 g.-mol.) in the solvent (10 c.c.) was mixed with a solution of urea (0·01 g.-mol.) in the same solvent (10 c.c.). When the solubility of the pyrimidine allowed, cold solutions were used and crystallisation of the complex followed almost immediately. Solutions of the less soluble pyrimidines were mixed with the urea solution at the boil; the mixture was cooled quickly without shaking, and allowed to crystallise as far as possible at room temperature. The *complex* crystallised in a pure state and was collected, washed, and dried.

Complexes of Urea with Pyrimidines in a Ratio other than Equimolecular (*see Table* 2).—A complete solution of urea and the pyrimidine was obtained at the boil, a minimum of 10 c.c. of solvent being used per g. of urea. The filtered solution was cooled quickly, and the *complex* allowed to crystallise.

Complexes of 2-*Hydroxy*-4 : 6-*dimethylpyrimidine with Compounds related to Urea* (*see Table* 3). —The method followed was essentially that just described.

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