PYRIMIDINES.

75.* SYNTHESES BASED ON ACETYLPYRIMIDINES. 4,6-DIHYDROXY-5-ACETYLPYRIMIDINE AND PREPARATION OF 4',5-BIPYRIMIDINES AND THEIR DERIVATIVES

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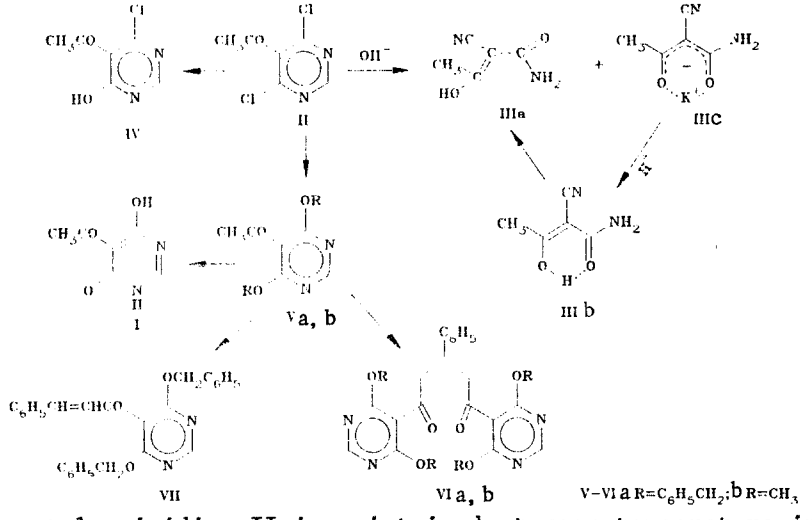
4,6-Dihydroxy-5-acetylpyrimidine was obtained by the solvolysis of 4,6-dialkoxy-5-acetylpyrimidines. The hydrolysis of 4,6-dichloro-5-acetylpyrimidine leads to opening of the heteroring to give s-cis,trans conformers of 2-cyano-3-hydroxy-2-buteneamide. 2',4,6-Trihydroxy[4',5]bipyrimidine was obtained by the condensation of 4,6-dialkoxy-5-acetylpyrimidines with benzalbisurea. It is shown that the products of the reaction of the same ketones with benzaldehyde in the presence of sodium alkoxides are derivatives of δ-diketones.

It has been previously shown that the condensation of 5-acetyluracil with benzalbisurea gives 2,2',4-trihydroxy[4',5]bipyrimidine [2], which is readily converted to the corresponding 2,2',4-trichlorobipyrimidine [3]. In a continuation of this research we attempted to synthesize 4',5-bipyrimidines with a 2',4,6 orientation of the substituents, as well as the necessary starting compound 4,6-dihydroxy-5-acetylpyrimidine (I).

For the synthesis of dihydroxypyrimidine I, as the starting compounds we selected 4,6-dichloro- (II) [4] and 4,6-dialkoxy-5-acetylpyrimidines, inasmuch as the preparation of 4,6-dihydroxypyrimidines from 4,6-dichloro-5-nitro- [5, 6] and 4,6-dibenzyloxypyrimidines [7] is known. However, the process frequently stops at the step involving the more readily formed monohydroxy derivatives [5, 8] and may be complicated by opening of the pyrimidine ring [4].



When dichloroacetylpyrimidine II is maintained at room temperature in 10% KOH solution, the starting compound vanishes after 1 h (according to TLC data), and only the product of opening of the pyrimidine ring, viz., 2-cyano-3-hydroxy-2-buteneamide (III), is present in the reaction mixture. Amide III was isolated in two forms (IIIa,b), which have different melting points and spectral characteristics; with respect to its melting point and IR, PMR, and mass spectra, the IIIa form is identical to the compound described in [9]. The potassium salt of butenamide IIIc, which was isolated from the reaction mixture by careful acidifica-

*See [1] for Communication 74.

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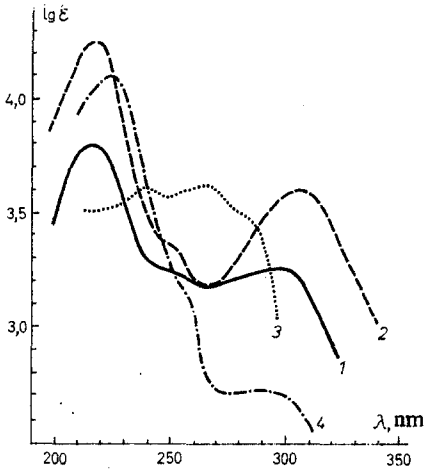

Fig. 1. UV spectra of the pyrimidines in alcohol: 1) ketone I; 2) 4,6-dihydroxy-5-formylpyrimidine; 3) 4,6-dihydroxypyrimidine; 4) 5-acetylpyrimidine.

tion, gives IIIb, which, upon recrystallization from alcohol, is converted to the more stable form IIIa. The enumerated data constitute evidence that amide III is produced in the form of s-cis and s-trans conformers: The higher-melting and stable IIIa form is the s-trans conformer, and the lower-melting form with a much lower νC=O intensity in the IR spectrum is the s-cis conformer [10]. It is interesting to note that in the case of the IIIb conformer the CN group shows up in the IR spectrum as a doublet.

The hydrolysis of dichloropyrimidine II by refluxing in a mixture of 10% HCl and dioxane leads to 4-chloro-6-hydroxy-5-acetylpyrimidine (IV), whereas in the case of refluxing with 10% HCl, according to the mass-spectrometric data, it leads to a mixture of dihydroxypyrimidine I and chlorohydroxypyrimidine IV. In both cases one observes a substantial degree of opening of the ring to give amide III, and the yields of the hydrolysis products are very low.

In order to study the possibility of obtaining pyrimidine I by catalytic debenzylation we synthesized 4,6-dibenzyloxy-5-acetylpyrimidine (Va). We found that VIa is also formed in the preparation of ketone Va by the reaction of dichloro ketone II with sodium benzylate. According to the mass-spectrometric data, VIa has a mass of 738.2803 and an empirical formula $C_{47}H_{38}N_4O_5$, and this may correspond to a 4H-pyran derivative. However, this assumption was not confirmed by other spectral characteristics, viz., the position of the C=O band in the IR spectrum and the presence of complex multiplet signals at strong field in the PMR spectrum. In conformity with the information presented above, VIa is a δ-diketone: The character of the PMR spectrum of the latter at 2-4 ppm is very similar to the spectrum of 1,3,5-triphenyl-1,5-pentanedione [11]. Diketone VIa could have been formed with the participation of the benzaldehyde that is present as an impurity in the benzyl alcohol. The corresponding diazachalcone VII, which may also be formed under the conditions used, was not detected in the reaction mixture. This may be explained by subsequent Michael condensation of the initially formed (from ketone Va and benzaldehyde) diazachalcone VII with a second molecule of acetylpyrimidine Va, which is a known method for the preparation of δ-diketones [12]. Similarly, only δ-diketone VIb was also obtained from acetylpyrimidine Vb and benzaldehyde in the presence of sodium methoxide. Diazachalcone VII is the product of the reaction of acetylpyrimidine Va and benzaldehyde when NaOH is used as the condensing agent. It follows from the IR spectra of KBr pellets and solutions in $CHCl_3$ and the data in [2, 13] that VII exists in the s-cis form (νC=O 1650 cm^{-1}). although the s-trans conformer (νC=O 1625 cm^{-1}) is also present under these and other conditions (to a greater extent in $CHCl_3$).

Dibenzyloxy derivative Va is obtained smoothly by oxidation of 4,6-benzyloxy-5-(α-hydroxyethyl)pyrimidine (VIII), and both compounds undergo catalytic debenzylation. The product of the catalytic hydrogenolysis of pyrimidine Va is IX, the molecular mass of which is two units greater than that of ketone I.

TABLE 1. PMR Spectra of the Synthesized Pyrimidines I, III-IX, and XI-XV

Compound	Solvent	Chemical shifts, δ, ppm (J, Hz)					
		CH_3	CH_2	H_{arom}	pyrimidine 2-H	NH_2, NH or OH	other signals
I	d_6-DMSO	2,70 (s, 3H)	—	—	8,89	9,89 br	—
IIIa	d_6-DMSO	2,20 (s, 3H)	—	—	—	9,17 br	—
IIIb	d_6-DMSO	2,17 (s, 4H)[a]	—	—	—	9,07 br	2,17 (CH)[a]
IIIc	D_2O[b]	2,30 (s, 3H)	—	—	—	2,40 (s, 2H)	—
IV	D_2O	2,73 (s, 3H)	—	—	8,53	—	—
	DMSO	—	—	—	8,40	11,03	6,60 br., 7,43
Va	CCl_4	2,33 (s, 3H)	5,33 (s, 4H)	7,23 (m, 10H)	8,27	—	—
Vb	d_6-Acetone	2,33 (s, 3H); 3,90 (s, 6H)	—	—	8,37	—	—
VIa	d_6-Acetone	—	2,65—3,10 (m, 5H)[a]; 5,30 (s, 8H)	6,93 (s, 5H); 7,20 (s, 20H)	8,33	—	CH[a]
VIb	$CDCl_3$	3,30—4,0 (m, 13H)[a]	2,5—3,3 (m, 4H)	7,10 (m, 5H)	8,34	—	CH[a]
VII	DMSO+ +$CDCl_3$	—	5,43 (s, 4H)	7,18—7,36 (m, 17H)[a]	8,46	—	H_{vinyl}[a] 5,25 (m, 1H, J_1=6,5, J_2=9, CH)
VIII	d_6-Acetone	1,40 (d, 3H, J_1=6,5)	5,43 (s, 4H)	7,33 (m, 10H)	8,27	3,57 (d, 1H, J_2=9, OH)[c]	
IX	d_6-DMSO	2,33 (s, 3H)	4,33 (s, 2H)	—	—	7,53 (1H); 8,43 (1H)	3,30 br (CH)
XI	d_6-DMSO	—	—	7,47 (m, 3H)[d]; 7,93 (m, 2H)[d]	8,37	14,2 br	7,77 (s, 1H, 5′-H_{pyrim})
XII	d_6-DMSO	—	—	8,20 (m, 3H)[d]; 8,80 (m, 2H)[d]	9,83	—	9,17 (s, 1H, 5′-H_{pyrim})
XIII	d_6-DMSO+ +CH_3OH	2,87 (s, 6H, NCH_3); 3,87 (s, 6H, OCH_3)	—	—	8,47	—	5,13 and 7,23 (d, each 1H, J=12, H_{vinyl})
XIV	d_6-Acetone	1,20 (t, 6H)	4,40 (q, 4H)	7,40 (m, 4H)[a,d]; 8,40 (m, 3H)[a,e]	8,40[a]	—	7,40 (5′-H_{pyrim});[a] 8,80 (d, 1H, J=5, 6′-H_{pyrim})
XV	d_6-DMSO	3,83 (s, 6H)	—	—	8,47	—	6,53 (d, 2H, J=5); 8,20 (d, 2H, J=5)

[a]Signals are superimposed. [b]Tetramethylsilane (TMS) as the external standard. [c]Vanishes when methanol is added. [d]m,p-H_{arom}. [e]o-H_{arom}.

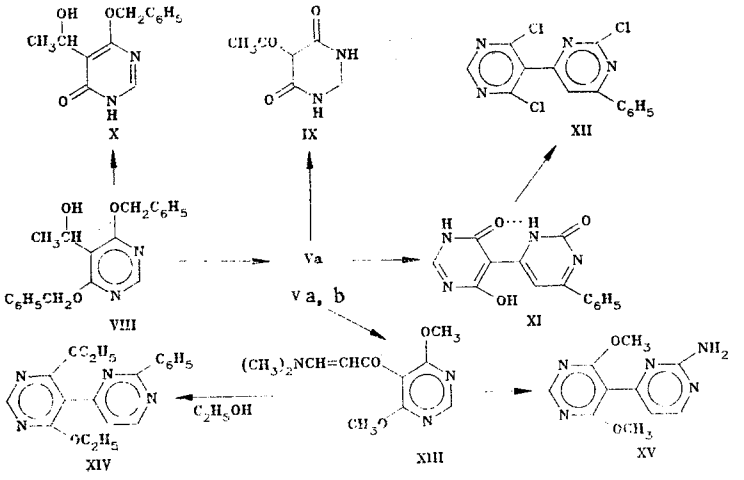

TABLE 2. Physicochemical Characteristics of I and III-XV

Compound	mp, °C (solvent)	R_f	UV spectrum, λ_{max}, nm (log ε) (in alcohol)	IR spectrum, ν, cm^{-1} (in KBr)	Found, %			Empirical formula	Calc., %			M [M]	Yield, %
					C	H	N(Cl)		C	H	N(Cl)		
I	300	—	210 (3,48), 250 sh (3,02), 294 (2,92), 390 (2,38)[a]	1530, 1580—1700, 1740[b]	—	—	—	$C_6H_6N_2O_3$	—	—	—	154,0383	22
IIIa	170—176, subl. (171—173° [8])	0,19	201 (4,13), 257 (4,23)	1595—1610, 1670, 2225, 3245, 3285, 3345, 3400	—	—	—	$C_5H_6N_2O_2$	—	—	—	126,0425	—
IIIb	110—120, subl.	0,15		1610, 1670, 2230, 2250, 3000—3200, 3390	—	—	—	$C_5H_6N_2O_2$	—	—	—	126,0422	40
IIIc	288—290 (alcohol)	—	—	1600, 2190, 2210, 3300, 3400	—	—	17,1[c]	$C_5H_5KN_2O_2$	—	—	17,0	—	78
IV	150—160	0,12	204, 234 sh, 280[d]	1540, 1590, 1660, 1710	—	—	—	$C_6H_5ClN_2O_2$	—	—	—	172,0022	11
Va	60—62 (alcohol)	0,79	207 (4,62), 248 (3,69)	1120, 1310, 1570, 1690, 1700	72,3	5,5	8,5	$C_{20}H_{18}N_2O_3$	71,9	5,5	8,4	243 [M−91]+	93
Vb	63—65 (pet. ether) 40—60°)	0,59	204 (4,37), 247 (3,78)	1120, 1310, 1415, 1470, 1580, 1700	52,8	5,5	15,3	$C_8H_{10}N_2O_3$	52,7	5,5	15,4	182	84
VIa	113—115 (alcohol)	0,85	—	1710	74,9	5,4	7,5	$C_{47}H_{40}N_4O_6$	74,6	5,3	7,4	[M−18]+	31
VIb	144.5—145,5 (alcohol)	0,25	204 (4,47), 250 (4,06)	1710	60,9	5,3	12,5	$C_{23}H_{24}N_4O_6$	61,1	5,3	12,5	452	44
VII	105—108 (alcohol)	—	203 (4,72), 305 (4,38)	1605, 1625, 1650	—	—	6,6	$C_{27}H_{22}N_2O_3$	—	—	6,6	422	79
VIII	73—74 (pet. ether) 70—100°)	0,67	245 (3,83)	1105, 1460, 1570, 3400	71,4	5,9	8,3	$C_{20}H_{20}N_2O_3$	71,4	5,9	8,3	336	71
IX	235—240 (alcohol)	—	268 (4,14)[a]	1590, 1640—1690, 2860, 3250, 3420	—	—	—	$C_6H_8N_2O_3$	—	—	—	156,0518	78
X	300	—	—	1650—1670	—	—	—	$C_{13}H_{13}N_2O_3$	—	—	—	245,0923 [M−1]+	36
XI	260, dec. (H_2O)	—	222 (4,16), 265 (3,88), 390 (4,19)	1560—1630	—	—	—	—	—	—	—	—	48
XII	198—200, subl.	0,77	259 (4,15), 294 (4,28)	1400, 1510, 1590	49,6	2,1	16,4 (31,2)	$C_{14}H_7Cl_3N_4$	50,0	2,1	16,7 (31,2)	336	20
XIII	223—224 (alcohol)	0,18	247 (3,89), 308 (4,40)	1580, 1600, 1630	55,5	6,1	18,0	$C_{11}H_{15}N_3O_3$	55,7	6,3	17,7	237	92
XIV	72—75	0,55	259 (4,39)	1120, 1310, 1440, 1580	—	—	—	$C_{18}H_{16}N_4O_2$	—	—	—	322,1425	37
XV	192—195	0,16	201 (4,35), 231 (4,06), 307 (4,07)	1125, 1300, 1400, 1480, 1580, 1640, 3180, 3320, 3390	—	—	—	$C_{10}H_{11}N_5O_2$	—	—	—	233,0908	61

[a]In water. [b]In mineral oil. [c]Ash content 33.3%. [d]Very slightly soluble.

In the IR spectrum of this compound one observes intense absorption at 1600-1700 cm^{-1}, and a signal of a CH_2 group and a broad signal at 3.30 ppm, which does not vanish when deuterated methanol is added, are present in the PMR spectrum; this makes it possible to assign it to the signal of the $>CH-$ group. The presence of the indicated additional signals in the PMR spectrum constitutes evidence for reduction of the pyrimidine ring in the catalytic debenzylation of pyrimidine Va at the 2–3 bond to give 4,6-dioxo-5-acetylhexahydropyrimidine (IX). A similar result was obtained in [7]. Only 4-hydroxy-6-benzyloxy-5-(α-hydroxyethyl)-pyrimidine (X) is formed in the catalytic debenzylation of pyrimidine VIII.

Another method for the synthesis of dihydroxypyrimidine I is dealkylation of dialkoxypyrimidines V. In the hydrolytic cleavage of 4,6-dibenzyloxy-5-methylpyrimidine [7] one group is readily hydrolyzed, and both benzyl groups can be removed only by prolonged heating in ampuls with excess HCl.

We were able to accomplish the dealkylation of acetylpyrimidines V by heating them in a solution of hydrogen chloride in n-butanol. The resulting 4,6-dihydroxy-5-acetylpyrimidine (I) is a compound with a high melting point and is virtually insoluble in water and alcohol. According to the data in [14] for 5-substituted (without a carbonyl group) 4,6-dihydroxypyrimidines, of the tautomeric forms, the preponderant form is the dipolar-ionic form (in water) or in the hydroxy-oxo form [in dimethyl sulfoxide (DMSO), alcohol], which have characteristic UV spectra. The UV spectrum of ketone I remains virtually unchanged on passing from water to alcohol, differs markedly from the spectrum of 4,6-dihydroxypyrimidine, has a more intense long-wave band as compared with 5-acetylpyrimidine [15], and is closest in the configuration of the bands to the UV spectrum of 4,6-dihydroxy-5-formylpyrimidine obtained by the method in [16]. At the same time, the IR spectra of KBr pellets of acetylpyrimidine I and its formyl analog differ markedly over the 1500-1700 cm^{-1} range by the presence in the latter of a clearly expressed absorption band of a formyl carbonyl group (1700 cm^{-1}). In the case of ketone I very broad absorption bands in the νC=O region are characteristic because of the superimposition of several bands, which makes it difficult to arrive at an assignment of them. This is possibly associated with the more active participation of the carbonyl group of the acetyl fragment in the tautomeric transformations (see [17]). The absence of a signal of a 5-H proton in the PMR spectrum of ketone I makes it possible to repudiate the concept of the preponderant possible tautomeric forms with an sp^3-hybrid carbon atom in the 5 position of the pyrimidine ring [14].

Inasmuch as the conditions found for the preparation of dihydroxyacetylpyrimidine I and the conditions under which acetyluracils and benzalbisurea to give bipyrimidines [2] were found to be similar, it was logical to use alkoxy derivatives V for the synthesis of 2',4,6-trihydroxypyrimidine derivatives rather than the more inaccessible ketone I; in this case one might have expected the simultaneous condensation and dealkylation of the alkoxy groups. In the reaction of ketones V with benzalbisurea in absolute n-butanol in the presence of HCl we observed the formation of a high-melting product, which we identified, on the basis of the spectral characteristics, as 4-hydroxy-2',6-dioxo-6'-phenyl-1,1',2',6-tetrahydro[4',5]bipyrimidine (XI). Its extremely low solubility in organic solvents and its low volatility did not make it possible to obtain an analytical sample and to determine its molecular mass, even by mass spectrometry. The structure of trihydroxypryimidine XI was confirmed by its conversion to the corresponding trichlorobipyrimidine XII by refluxing with $POCl_3$.

Ketone Vb reacts smoothly with dimethylformamide dimethylacetal to give enamino ketone XIII. The latter, in analogy with known reactions [18], via reaction with the amidine component, opens up the possibility of obtaining various 2',4,6-substituted [4',5]bipyrimidines. The condensation of enamino ketone XIII with benzylamine and guanidine leads to the formation of, respectively, 2'-phenyl- (XIV) and 2'-amino[4',5]bipyrimidines (XV).

EXPERIMENTAL

The IR spectra of the compounds were recorded with a UR-20 spectrometer, the UV spectra were recorded with a Specord UV-vis spectrophotometer, and the PMR spectra were obtained with a Varian A56/60A spectrometer with hexamethyldisoloxane (HMDS) as the internal standard. The molecular masses were determined with a high-resolution MS 902 mass spectrometer with a system for direct introduction of the samples at 120-140°C. Thin-layer chromatography (TLC) was carried out on Silufol UV-254 and KSK silica gel plates in a chloroform–ethanol system (30:1).

4,6-Dihydroxy-5-acetylpyrimidine (I). A 0.2-g (0.6 mmole) sample of ketone Va was added to a solution of 0.05 g (1.5 mmoles) of dry HCl in 2 ml of absolute n-butanol, and the mixture was refluxed for 2 h. It was then cooled and filtered. The filtrate was diluted with ether, and ketone I was removed by filtration.

2-Cyano-3-hydroxy-2-buteneamide (III). A 1.5-g (7.9 mmoles) sample of 4,6-dichloro-5-acetylpyrimidine in 45 ml of 10% KOH solution was stirred for 2 h, after which the light-yellow solution was acidified to pH 4 with 10% HCl and extracted with methylene chloride (five 20-ml portions). The extract was dried with $MgSO_4$ and evaporated, and the residue was sublimed at 80-100°C (2 mm) for 6 h to give 0.09 g of IIIa.

A 1.5-ml sample of concentrated HCl was added to a suspension of 0.7 g of salt IIIc in 27 ml of absolute ether, after which the KCl was removed by filtration, and the filtrate was evaporated. Sublimation of the residue at 110°C (2 mm) gave 0.4 g of amide IIIb. Recrystallization of IIIb from alcohol gave IIIa with mp 175-178°C.

4-Chloro-6-hydroxy-5-acetylpyrimidine (IV). A) A mixture of 1 g (5.5 mmoles) of pyrimidine II, 10 ml of 10% HCl, and 5 ml of dioxane was refluxed for 3.5 g with chromatographic monitoring of the course of the reaction. The reaction mixture was poured into a Petri dish and allowed to stand in a desiccator over KOH. The resulting solid residue was dissolved in a small amount of water, and the solution was allowed to stand for 1 h, after which 0.1 g of pyrimidine IV was removed by filtration.

B) A mixture of 0.5 g (2.6 mmoles) of pyrimidine II and 5 ml of 10% HCl was refluxed for 1 h, and the resulting solution was evaporated. The residue was dissolved in a small amount of water, and the aqueous solution was made alkaline to pH 8 with ammonium hydroxide and extracted with ether. The extract was washed with water, dried with $MgSO_4$, and evaporated to give 0.01 g of a product with mp 300°C. IR spectrum (KBr): 1540-1550 and 1660-1720 cm^{-1}. Mass spectrum: 172, 174 (M^+); 157, 159 $(M-15)^+$ (chloro hydroxy derivative IV); 154 (M^+) and 139 $(M-15)^+$ (dihydroxy derivative I).

4,6-Dibenzyloxy-5-acetylpyrimidine (Va). A mixture of 0.5 g (1.5 mmoles) of alcohol VIII and 5 g of active MnO_2 in 70 ml of methylene chloride was stirred at room temperature for 10 h, after which the MnO_2 was removed by filtration and washed with hot metylene chloride (five 40-ml portions). The combined solutions were evaporated, and the oily residue crystallized rapidly to give 0.46 g of ketone Va.

4,6-Dimethoxy-5-acetylpyrimidine (Vb). A solution of 1 g (5.2 mmoles) of pyrimidine II in 30 ml of methylene chloride was added dropwise with stirring to a solution of sodium methoxide [from 0.45 g (20 mmoles) of Na metal and 10 ml of absolute methanol], and the mixture was stirred at room temperature for 7 h. The NaCl was removed by filtration, and the filtrate was evaporated. The solid residue was treated with water, and the aqueous mixture was extracted with ether. The ether solution was dried with $MgSO_4$ and evaporated, and the residue was sublimed at 80°C (6 mm) to give 0.8 g of ketone Vb.

1,5-Bis(4,6-dibenzyloxy-5-pyrimidinyl)-3-phenyl-1,5-pentadione (VIa) and 4,6-Dibenzyloxy-5-acetylpyrimidine (Va). A solution of 1 g (5.2 mmole) of pyrimidine II in 20 ml of methylene chloride was added dropwise with stirring to a solution of sodium benzylate [from 0.45 g (20 mmoles) of sodium metal and 14 ml of dry benzyl alcohol], and the mixture was then stirred at room temperature for 2 h. The NaCl was removed by filtration, the filtrate was evaporated, and the residue was washed with petroleum ether to give 0.4 g of ketone Va with mp 59-62°C (from petroleum ether, 70-100°C). The filtrate was separated preparatively by thin-layer chromatography (TLC) to give 0.62 g of diketone VIa.

1,5-Bis(4,6-dimethoxy-5-pyrimidinyl)-3-phenyl-1,5-pentanedione (VIb). A 0.03-g (0.5 mmole) sample of sodium methoxide was dissolved in 0.5 ml of absolute methanol, 3 ml of absolute benzene, 0.53 g (2 mmoles) of ketone Vb, and 0.1 ml (1 mmole) of benzaldehyde were added, and the mixture was stirred at room temperature for 10 h and then allowed to stand overnight. It was subsequently evaporated to dryness *in vacuo*, and the residue was triturated with water and neutralized with 20% HCl. Trituration of the mixtrue was continued after decantation of the aqueous layer with the addition of new portions of water until a viscous mass was obtained. The latter viscous mass was triturated with 1 ml of alcohol, and the precipitate was removed by filtration and washed with ether to give 0.2 g of diketone VIb.

4,6-Dibenzyloxy-5-pyrimidinyl Styryl Ketone (VII). A 0.28-g (0.84 mmole) sample of acetylpyrimidine Va was dissolved in 4 ml of methanol, and 0.09 g (0.84 mmole) of benzaldehyde and 0.6 ml of concentrated NaOH solution were added, as a result of which the mixture

became slightly warmer, and a precipitate began to form immediately. The mixture was allowed to stand overnight at room temperature, and the precipitate was removed by filtration, washed with water, and dried to give 0.28 g of ketone VII.

4,6-Dibenzyloxy-5-(α-hydroxyethyl)pyrimidine (VIII). A solution of 2.4 g (12 mmoles) of 4,6-dichloro-5-(α-hydroxyethyl)pyrimidine [4] in 30 ml of methylene chloride was added dropwise with stirring to a solution of sodium benzylate [from 1.1 g (48 mmoles) of Na metal and 34 ml of benzyl alcohol], and the mixture was stirred at room temperature for 3 h. It was then diluted with 30 ml of water, and the aqueous mixture was extracted with ether. The organic layer was dried with $MgSO_4$ and evaporated *in vacuo*. The residue, which began to crystallize, was washed with petroleum ether (70-100°C) to give 3 g of alcohol VIII.

4,6-Dioxo-5-acetylhexahydropyrimidine (IX). A 0.2-g (0.6 mmole) sample of ketone Va was dissolved in 10 ml of ethanol and hydrogenated at atmospheric pressure and room temperature in the presence of 0.4 g of 5% Pd/C for 2 h. The solution was filtered, and the precipitate was washed with hot alcohol. The combined filtrates were evaporated to give 0.07 g of dihydroxypyrimidine IX.

4-Hydroxy-6-benzyloxy-5-(α-hydroxyethyl)pyrimidine (X). A 0.2-g (0.6 mmole) sample of alcohol VIII was hydrogenated at atmospheric pressure and room temperature in 7 ml of ethanol in the presence of 0.04 g of 5% Pd/C for 24 h. The solution was filtered, the precipitate was washed with hot alcohol, and the combined filtrates were evaporated to give 0.05 g of alcohol X.

4-Hydroxy-2',6-dioxo-6'-phenyl-1,1',2',6-tetrahydro[4',5]bipyrimidine (XI). A) A 0.34-g (1.7 mmoles) sample of benzalbisurea and 0.15 g (0.85 mmole) of ketone Vb were added to a solution of 0.059 g (1.7 mmoles) of dry HCl in 2.5 ml of absolute n-butanol, and the reaction mixture was refluxed for 3 h. It was then cooled, and the precipitate was removed by filtration and washed successivly with $NaHCO_3$ solution, water, and alcohol to give 0.11 g of bipyrimidine XI.

B) Similarly, from 0.2 g (0.6 mmole) of ketone Va and 0.25 g (1.2 mmoles) of benzalbisurea in n-butanol in the presence of 0.043 g (1.2 mmoles) of dry HCl we obtained 0.068 g (40%) of bipyrimidine XI with mp 260°C (from water).

2',4,6-Trichloro-6'-phenyl[4',5]bipyrimidine (XII). A mixture of 1.2 g (4.3 mmoles) of bipyrimidine XI, 8.5 ml of $POCl_3$, 0.85 ml of dimethylaniline, and three drops of water was refluxed for 10 h, after which the bulk of $POCl_3$ was removed by vacuum distillation, and the residue was poured over ice. The resulting aqueous mixture was extracted with benzene, and the benzene extracts were washed successively with $NaHCO_3$ solution and water, dried with $CaCl_2$, and evaporated. The residue was washed with diethyl ether and sublimed at 160°C (2 mm) to give 0.28 g of bipyrimidine XII.

4,6-Dimethoxy-5-[(β-dimethylaminomethylene)acetyl]pyrimidine (XIII). A mixture of 1.8 g (9.8 mmoles) of ketone Vb and 5 g (34 mmoles) of dimethylformamide diethylacetal was heated at 150-160°C for 16 h, after which it was cooled, and the precipitate was washed with absolute ether to give 2 g of aminomethylene ketone XIII.

4,6-Diethoxy-2'-phenyl[4',5]bipyrimidine (XIV). A 0.265-g (1.7 mmoles) sample of benzamidine hydrochloride was added to a solution of 0.4 g (1.7 mmoles) of methylene ketone XIII in 4 ml of absolute alcohol, after which, a solution of sodium ethoxide (from 0.08 g of Na metal in 4 ml of alcohol) was added dropwise with vigorous stirring at 80°C, and the mixture was stirred for 3 h. The NaCl was removed by filtration, and the filtrate was allowed to stand in a refigerator overnight. The precipitate was removed by filtration to give 0.2 g of pyrimidine XIV.

2'-Amino-4,6-dimethoxy[4',5]bipyrimidine (XV). A 0.38-g (2.1 mmoles) sample of guanidine carbonate was added to a solution of 1 g (4.2 mmoles) of ketone XIII in 15 ml of absolute methanol, and the mixture was heated to 60-70°C, at which point a solution of sodium methoxide (from 0.08 g of Na metal in 4.5 ml of absolute methanol) was added rapidly with vigorous stirring. The reaction mixture was stirred at 70-80°C for 7 h and then allowed to stand in a refrigerator overnight. The precipitate was removed by filtration and washed successively with alcohol and water to give 0.6 g of bipyrimidine XV.

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IODO- AND CHLORODEMERCURATION OF 5,5'-MERCURIBISURACILS

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The direct C mercuration in the 5 position of 1-acetyluracil by means of mercury(II) trifluoroacetate in anhydrous acetonitrile is described. The intermediately formed 1-acetyl-5-trifluoroacetoxymercuriuracil, without isolation, was subjected to symmetrization by the action of potassium iodide. The acetyl groups were then readily split out by the action of water. The resulting 5,5'-mercuribisuracil (50% yield) forms 5-iodo- or a 5-chlorouracil in 93% or 72% yields, respectively, under the influence of an aqueous KI_3 solution or excess pure liquid S_2Cl_2.

It is known that under the influence of mercury(II) acetate on caffeine [1, 2] or mercury(II) chloride on N_1,N_3-dimethyluracil [3] one observes the formation of their C-organomercury derivatives with substituents in the 8 or 5 positions, respectively. On the other hand, dimethyl-substituted xanthines [4, 5], imidazoles, uracils, etc. [6-8] generally give rather stable and, as a rule, slightly soluble metal complexes, or else the reaction stops at the stage involving the formation of slightly soluble N-organomercury derivatives (sometimes with admixed C-mercuri derivatives) [7, 8]. For example, uracil very rapidly forms a slightly soluble Hg complex [5, 6] in a ratio of 1:1; the latter is used in the syntheses of nucleosides [6, 9, 10]. Thus the fact is that, in the direct C mercuration of uracil, it is expedient to temporarily protect the N_1 position by means of some readily eliminable residue such as the very easily removable acyl group [17]. It has been demonstrated [11] that a methyl group is not at all applicable in this case and that benzyl and benzyloxy-

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