Amino-5-(diphenylmethyl)-1,3-dimethyluracil (22 and 23). 6-Amino-1,3-dimethyluracil (15.5 g or 0.1 mol) and benzhydrol (19.8 g or 0.1 mol) were heated under reflux for 6 hr in 100 ml of glacial acetic acid. The cooled solution was added to water. The precipitated solid was collected and was crystallized from methanol to yield 20 g or 65% of 5-(diphenylmethyl)-1,3-dimethylbarbituric acid (**22**), mp 167–168°.

Anal. Calcd for $C_{19}H_{18}N_2O_3$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.73; H, 5.77; N, 8.82.

The methanol filtrate from the above crystallization was concentrated to give 6-amino-5-(diphenylmethyl)-1,3-dimethyluracil (**23**) that melted at 225° after several recrystallizations, yield 5 g or 15.5%.

Anal. Calcd for $C_{19}H_{19}N_3O_2$: C, 71.01; H, 5.96; N, 13.08. Found: C, 71.08; H, 5.93; N, 12.87.

5-(Xanthen-9-yl)- and 5-(10,11-Dihydro-5*H*-dibenzo[*a,d*]cyclohepten-5-yl)pyrimidines (24, 26, 28, 29) (Table III). To 0.1 mol of barbituric acid, 4,6-dihydroxypyrimidine, or cytosine in 200 ml of glacial acetic acid was added 0.1 mol of xanthen-9-ol. A dark blue color developed almost immediately upon heating and appeared to become less intense as the reaction proceeded. The alkylation was rapid and by all indications was complete within 15 min. The reflux temperature was maintained for 1–2 hr and the cooled mixture then diluted with water. The solid products were crystallized from alcohol or a mixture of alcohol and DMF.

Uracil (0.2 mol) and barbituric acid (0.2 mol) in HOAc were separately heated with 0.2 mol of 10,11-dihydro-5*H*-dibenzo[*a,d*]-cyclohepten-5-ol and 20 g of boron trifluoride etherate. After 3–5 hr the products were isolated as described above and crystallized from alcohol.

2-Diarylmethylmalondiamides (30 and 31) (Table IV). Malondiamide (0.05 mol) and the appropriate diarylcarbinol (0.05 mol) were dissolved in 20 ml of hot 100% formic acid. Five drops of boron trifluoride etherate were added and the solution was heated under reflux for 10–12 min and then cooled. The solid product, precipitated by adding cold water, was washed with water and with ether and then crystallized from alcohol.

2-Diarylmethyl-, 2-(Xanthen-9-yl)-, and 2-Triphenylmethylmalononitriles (32–35) (Table IV). The diarylmethylmalondiamides (**30** and **31**) previously decribed were dehydrated by heating 0.1 mol of the diamide with 35–45 ml of $POCl_3$ in 25 g of acetamide for 3 hr at the refluxing temperature. The reaction mixture was poured onto ice and extracted into ether. The ether solution was washed with water, dried, and evaporated to yield the crystalline products (**32** and **33**).

Malononitrile (0.11 mol) was heated with triphenylcarbinol (0.1 mol) or with xanthen-9-ol (0.1 mol) in 50 ml of acetic acid. The reaction with xanthen-9-ol was complete in about 2 min, while the mixture containing triphenylcarbinol was heated for 8 hr. The cooled mixtures were added to water and the precipitated solids then crystallized from benzene.

Cyclizations of 2-(Diphenylmethyl)- and 2-(2,4-Dichloro)diphenylmethylmalondiamides (12 and 13) (Table V). The 2-diarylmethylmalondiamide, **30** and **31** (0.1 mol), was heated in a mixture of formamide and DMSO containing 2.2 molar equivalents of either potassium *tert*-butoxide, sodium methylate, or sodium hydroxide. The products were precipitated by adding very dilute HCl. The 5-diarylmethyl-4,6-dihydroxypyrimidines were separated from unreacted 2-diarylmethylmalondiamides by crystallization from alcohol.

Registry No.—3, 40016-23-7; **4,** 50278-30-3; **5,** 50278-31-4; **6,** 50278-32-5; **7,** 50278-33-6; **8,** 50454-83-6; **9,** 50278-34-7; **10,** 50278-35-8; **11,** 50278-36-9; **12,** 50278-37-0; **13,** 50278-38-1; **14,** 50278-39-2; **15,** 26920-22-9; **16,** 50278-41-6; **17,** 50278-42-7; **18,** 50278-43-8; **19,** 50278-44-9; **20,** 50278-45-0; **21,** 50278-46-1; **22,** 50454-84-7; **23,** 50278-47-2; **24,** 50278-48-3; **25,** 50278-49-4; **26,** 50278-50-7; **27,** 50278-51-8; **28,** 50278-52-9; **29,** 50278-53-0; **30,** 13023-11-5; **31,** 50278-55-2; **32,** 1846-19-1; **33,** 50278-57-4; **34,** 6235-15-0; **35,** 50278-59-6; 2-hydroxypyrimidine, 2209-57-6; 4-hydroxypyrimidine, 4562-27-0; 2-thiopyrimidine, 1450-85-7.

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(8) D. J. Brown, "The Pyrimidines," Interscience, New York, N. Y., 1962, p 7.
(9) J. B. Campbell, C. W. Whitehead, T. J. Kress, and L. L. Moore, presented at the 4th Conference on Catalytic Hydrogenation and Analogous Pressure Reactions. New York Academy of Sciences, 1972.
(10) Satisfactory microanalytical data were obtained for the compounds in Tables I–IV.

Reactions of Diarylmethyl Cations with Aminopyrimidines

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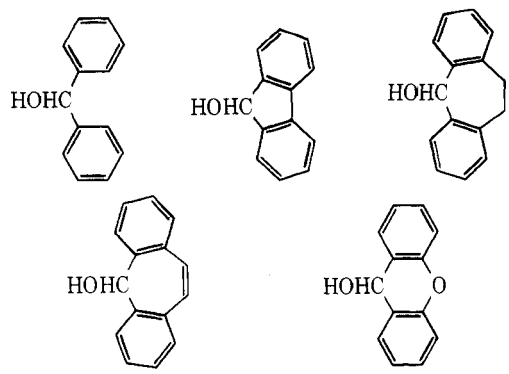
The reactions of diarylmethyl and dibenzomethyl cations with aminopyrimidines were investigated to determine the relative reactivities of the pyrimidine nucleophilic centers. While diarylmethyl cations reacted at the amine nitrogen of 2-aminopyrimidine, the diphenylmethyl cation reacted at both amine nitrogens of 4,6-diaminopyrimidine. Condensed dibenzomethyl cations reacted with 2-aminopyrimidine at the 2-amine nitrogen and at the 5-carbon position. The 9-xanthene cation reacted only at the 5 position of 4,6-diaminopyrimidine to yield 4,6-diamino-5-xanthen-9-ylpyrimidine. The relative affinity for these two positions is discussed. The 2-amino-4,6-dichloropyrimidine, substituted at the 5 position by diarylmethyl cations with accompanying hydrolysis of one chlorine, yields 2-amino-6-chloro-5-(diarylmethyl)-4-hydroxypyrimidines. A novel amino displacement of a 2-hydroxy group was apparently facilitated by the presence of the 5-(diphenylmethyl) group. Diphenylmethyl cation reacted with 4-amino-6-chloropyrimidine, followed by hydrolysis of the chlorine, to yield a mixture of 4-amino-5-(diphenylmethyl)-6-hydroxypyrimidine and 4-[(diphenylmethyl)amino]-6-hydroxypyrimidine.

Investigations in these laboratories have shown that 5-(diarylmethyl)pyrimidines have important antimicrobial as well as plant growth regulating properties.[1,2] Explorations into possible novel synthetic routes to these compounds led to this study of aralkylations of pyrimidines. Electrophilic substitutions by arylmethyl cations were shown, in the previous paper, to occur at the 5-carbon atom when the electron density of that position was enriched by hydroxy groups adjacent to nuclear nitrogens. While amino groups have electronic effects qualitatively similar to hydroxy groups, all previously reported alkylations of aminopyrimidines occurred at a nitrogen atom.[3,4]

Substitutions of aminopyrimidines by diarylmethyl cations are not only influenced by the electron densities of the nucleophilic centers but also by the nature of the attacking carbonium ion. Aminopyrimidines were allowed to

react with an appropriate diarylcarbinol in boiling glacial acetic acid. The compounds 2-aminopyrimidine and 2-amino-4,6-dimethylpyrimidine reacted with benzhydrol, 4-chlorobenzhydrol, 2-methoxybenzhydrol, and 3,4,5-trimethoxybenzhydrol to give the corresponding 2-[(diphenylmethyl)amino]- or 2-substituted-[(diphenylmethyl)amino]-pyrimidines, compounds 1–12 (Table I). The nmr data were consistent with the assigned structures, and tlc of the reaction mixtures indicated they were the only products formed. Addition of bromine to an acetic acid solution of 2-[(diphenylmethyl)amino]pyrimidine readily yielded 5-bromo-2-[(diphenylmethyl)amino]pyrimidine (13). Triphenylcarbinol failed to react with 2-aminopyrimidine after 18 hr.

Condensed dibenzomethyl cations, depending upon their structure, react with 2-aminopyrimidine at either the 2-amino nitrogen or 5-carbon position to give a mixture of two products, or they react exclusively at the 5-carbon position. Xanthen-9-ol and 5*H*-dibenzo[*a*,*d*]cyclohepten-5-ol reacted only at the 5 position to yield, respectively, 2-amino-5-xanthen-9-ylpyrimidine (14) and 2-amino-5-(5*H*-dibenzo[*a*,*d*]cyclohepten-5-yl)pyrimidine (15). When reacted with 2-aminopyrimidine, 10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptа-1,4-dien-5-ol yielded a mixture of 2-(10,11-dihydro-5*H*-dibenzo[*a*,*d*]cyclohepta-1,4-dien-5-ylamino)pyrimidine (6) and 2-amino-N^2,5-bis-(10,11-dihydro-5*H*-dibenzo[*a*,*d*]cyclohepta-1,4-dien-6-yl)-pyrimidine (16). In the presence of excess 2-aminopyrimidine, 6 was formed exclusively. Reacting slowly with only the 2-amino group, 9-hydroxyfluorene gave after 24 hr starting material and 2-[(fluoren-9-yl)amino]pyrimidine (1) in 8% yield. The relative specificity for the 2-amino or 5-carbon position appears below.



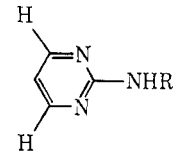
2-amino position ⟷ 5-carbon position

Benzhydrol reacted at both amino groups of 4,6-diaminopyrimidine to give a small yield of 4,6-bis[(diphenylmethyl)amino]pyrimidine (17). An nmr spectrum of the crude reaction mixture indicated the presence of unreacted 4,6-diaminopyrimidine. Xanthen-9-ol reacted with 4,6-diaminopyrimidine only at the 5 position to give 4,6-diamino-5-xanthen-9-ylpyrimidine (18) in good yield, but after 64 hr 9-hydroxyfluorene failed to react with 4,6-diaminopyrimidine. Xanthen-9-ol is oxidized completely to xanthen-9-one when dissolved in acetic acid at room temperature and allowed to stand for 15 min. Reactions of xanthen-9-ol with 2-aminopyrimidine or with 4,6-diaminopyrimidine must be completed rapidly upon contact.

Pyrimidine and pyrimidine sulfate each decomposed when heated in glacial acetic acid with benzhydrol. The only isolated product was (diphenylmethyl)acetamide. Xanthen-9-ol failed to react with pyrimidine at lower temperatures, and xanthen-9-one was obtained.

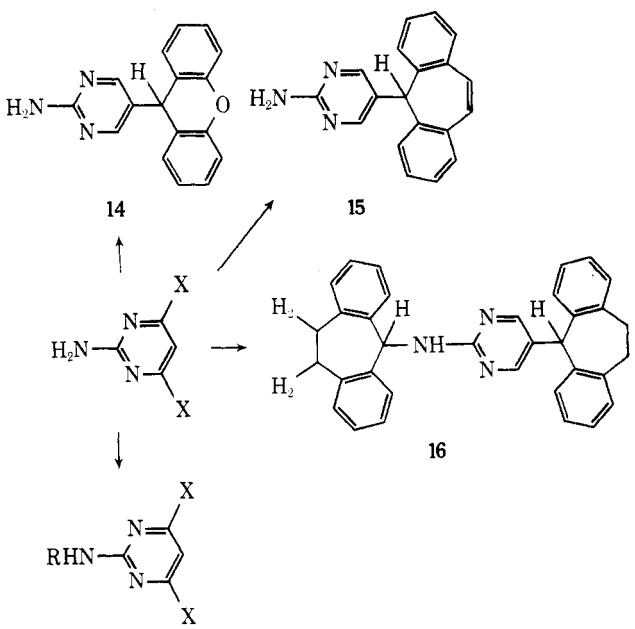
Both benzhydrol and 2-methoxybenzhydrol reacted at the 5 position of 2-amino-4,6-dichloropyrimdine. One of the chlorine atoms of 2-amino-4,6-dichloropyrimidine was

Table I
2-[(Diarylmethyl)amino]pyrimidines



No.	R	R_1	% yield[a]	Mp, °C[b,c]
1	$C_{14}H_{11}$[d]	H	8	200–201
2	$(4\text{-}ClC_6H_4)_2CH$	H	36	179–180
3	$4\text{-}ClC_6H_4C_6H_5CH$	H	49	127
4	$(C_6H_5)_2CH$	H	58	160[e]
5	$2\text{-}CH_3OC_6H_4C_6H_5CH$	H	50	149
6	$C_{15}H_{13}$[f]	H	71	175–177
7	$(4\text{-}ClC_6H_4)_2CH$	CH_3	21	125–127
8	$4\text{-}ClC_6H_4C_6H_5CH$	CH_3	31	118
9	$(C_6H_5)_2CH$	CH_3	62	126–127
10	$2\text{-}CH_3OC_6H_4C_6H_5CH$	CH_3	50	165–166
11	$3,4,5\text{-}(CH_3O)_3C_6H_2C_6H_5CH$	H	71	150
12	$3,4,5\text{-}(CH_3O)_3C_6H_2C_6H_5CH$	CH_3	51	158–59

[a] All yields were determined from analytically pure compounds. [b] The melting points are corrected. [c] Satisfactory analytical data (±0.4% for C, H, N, etc.) were reported for all new compounds listed in the paper. [d] Fluoren-9-yl. [e] Lit. mp 145–246° (19). [f] 10,11-Dihydro-5*H*-dibenzo[*a*,*d*]-cyclohepta-1,4-dien-5-yl.



1–12, X = H and CH_3.

R = fluoren-9-yl (X = H only); $(4\text{-}ClC_6H_4)_2CH$; $(4\text{-}ClC_6H_4)(C_6H_5)CH$; $(C_6H_5)_2CH$; $(2\text{-}CH_3OC_6H_4)(C_6H_5)CH$; 10,11-dihydro-5*H*-dibenzo[*a*,*d*]cyclohepta-1,4-dien-5-yl (X = H only); $(3,4,5\text{-}(CH_3O)_3C_6H_2)(C_6H_5)CH$

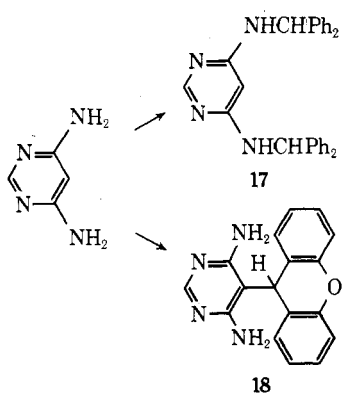
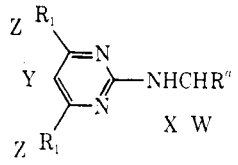


Table II
Nmr Data for the [(2-Diarylmethyl)amino]pyrimidines



Compd no.	R_1	Chemical shifts δ, ppm[b] W[d]	X[d]	Y	Z
1[c]	H	6.31	7–8	6.69[f]	8.35[d]
2	H	6.40	7.57	6.53[f]	8.17[d]
3	H	6.34	*g*	6.37[f]	7.94[d]
4	H	6.43	*g*	6.28[f]	7.87[d]
5	H	6.61	*g*	6.33[f]	8.02[d]
6	H	6.73	*g*	6.29[f]	8.05[d]
7	CH_3	6.45	7.73	6.28[e]	2.23[e]
8	CH_3	6.38	5.76	6.28[e]	2.20[e]
9	CH_3	6.51	*g*	6.20[e]	2.17[e]
10	CH_3	6.67	6.11	6.23[e]	2.21[e]
11	H	6.38	7.92	6.35[f]	7.87[d]
12	CH_3	6.35	6.73	6.28[e]	2.23[e]

[a] R represents two aryl groups (compounds **2–5, 7–12**) or two condensed aryl groups (compounds **1** and **6**). [b] The solvent was $CDCl_3$, unless otherwise designated. [c] Solvent was $(CD_3)_2SO$. [d] Doublet. [e] Singlet. [f] Triplet. [g] Under aromatic region.

hydrolyzed during the substitution reaction to give 2-amino-6-chloro-5-(diphenylmethyl)-4-hydroxypyrimidine (**19**) and 2-amino-6-chloro-4-hydroxy-5-[2-methyoxy(diphenylmethyl)]pyrimidine (**20**), respectively. When warmed in acetic acid, 2,4,6-trichloropyrimidine did not react with xanthen-9-ol and the trichloropyrimidine was not hydrolyzed under these conditions. This result and the fact that 2-amino-6-chloro-4-hydroxypyrimidine reacted with benzhydrol to yield compound **19** suggest that one chlorine of 2-amino-4,6-dichloropyrimidine is hydrolyzed before substitution occurs. The hydrolysis of one of the chloro groups of 2-amino-4,6-dichloropyrimidine and the unreactivity of the trichloropyrimidine might also be attributed to a greater degree of protonation in the 2-aminopyrimidine. Since **19**, when treated with nitrous acid,

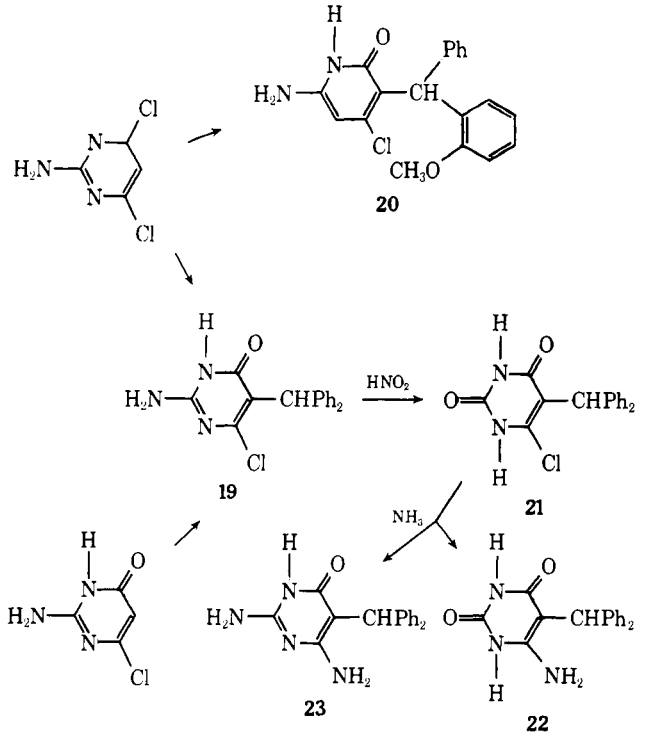
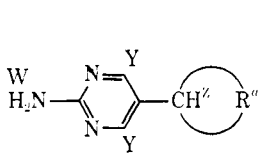
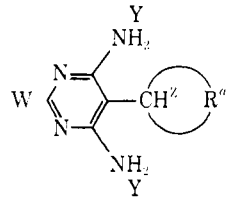


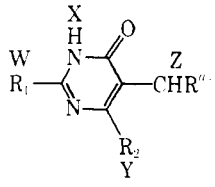
Table III
Nmr Data for [Amino(diarylmethyl)]pyrimidines



14 and 15



18

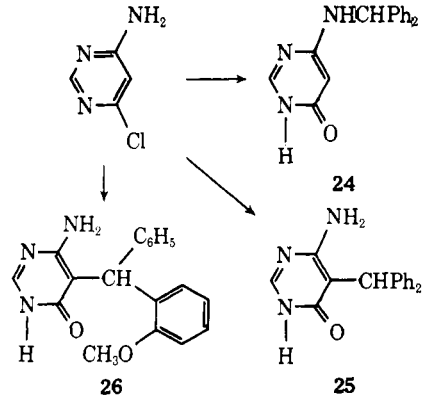


19-23

Compd no.	R_1	R_2	Chemical shifts δ, ppm W	X[b]	Y	Z[g]
14[c]			6.05		8.05[g]	5.16
15[c]			11.50		7.63[g]	5.44
18[d]			8.34[g]			5.92
19[e]	NH_2	Cl	6.97[b]	11.18		5.70
20[f]	NH_2	Cl	6.57[b]	11.00		6.00
21[c]	HO	Cl	6.62	6.62		5.70
22[e]	HO	NH_2	9.93[b]	10.38	5.78[b]	5.47
23[f]	NH_2	NH_2	5.34[b]	9.93	6.11[b]	5.61

[a] R represents two aryl groups (compounds **19–23**) or two condensed aryl groups (compounds **14, 15,** and **18**). [b] Broad signal. [c] Solvent was $CDCl_3$ + $(CD_3)_2SO$. [d] Compound was soluble only in trifluoroacetic acid; the NH_2 proton signals could not be observed. [e] Solvent was $(CD_3)_2SO$. [f] Solvent was $CDCl_3$. [g] Singlet.

yielded 4-chloro-2,6-dihydroxy-5-(diphenylmethyl)pyrimidine (**21**), the possibility that the diphenylmethyl group might have been on the 2-amino position was eliminated. When **21** was treated with alcoholic ammonia at 150°, the 6-chlorine was displaced with NH_2 to yield 6-amino-5-(diphenylmethyl)-2,4-dihydroxypyrimidine (**22**). Unexpectedly the 2-hydroxy group exchanged with ammonia to give a second product, 2,6-diamino-5-(diphenylmethyl)-4-hydroxypyrimidine (**23**). By comparing the nmr spectra of compounds **19** and **23**, it became obvious that the diarylmethyl group was on the 5-carbon. Exchange of the 2-hydroxy group with ammonia is facilitated by the presence of this 5-(diphenylmethyl) group, since 6-aminouracil remained unchanged when treated with alcoholic ammonia at 150°. The reaction of benzhydrol with 4-amino-6-chloropyrimidine yielded a mixture of 4-amino-5-(diphenylmethyl)-6-hydroxypyrimidine (**24**) and 4-[(diphenylmethyl)amino]-6-hydroxypyrimidine (**25**). Hydrolysis of the 6-chlorine also occurred in the reaction of 4-amino-6-chloropyrimidine with 2-methoxybenzhydrol, but only one prod-



uct, 4-amino-6-hydroxy-5-[2-methoxy(diphenylmethyl)]pyrimidine (**26**) was isolated.

Confirmation of Structures by Nmr Spectra

Signals for protons at the 4, 5, and 6 positions of compounds **1–6** and **11**, as well as signals for protons of the 4- and 6-methyl groups of compounds **7–10** and **12**, are given in Table II. Singlet signals at 6.20–6.28 ppm (Y, Table II) are from protons at position 5 when methyl groups are at both the 4 and 6 positions. Protons at positions 4 and 6 split the signals for protons at position 5 by 5 Hz, and the resulting triplets have centers at 6.28–6.53 ppm. Protons at positions 4 and 6 are less shielded and have doublet signals with centers at 7.87–8.17 ppm, split 5 Hz by a proton at position 5. The signal for 4- and 6-methyl protons occurs at 2.17 and 2.23 ppm (Z, Table II).

The doublet signals between 6.34 and 6.67 ppm (Y, Table II) for the CH protons of the diarylmethyl groups are split 8 Hz by the adjacent 2-amino proton.

The high field position of signals at 5.16–6.00 ppm (Z, Table III) and their singlet character show that compounds **14–19** and **21–23** have the diarylmethyl group at the 5 position.

Experimental Section

All melting points are corrected. The nmr spectra were determined by the Varian HA-60 instrument.

2-[(Diarylmethyl)amino]pyrimidines (Table I, Compounds 1–12). 2-Aminopyrimidine or 2-amino-4,6-dimethylpyrimidine (0.1 mol) and 0.1 mol of the appropriate diarylcarbinol were dissolved in 100 ml of glacial acetic acid. The solution was heated under reflux for 8 to 24 hr, cooled, and poured into water. The solid products were washed thoroughly with water, and the oily products were extracted into ether. The ether solution was washed with water, concentrated, and eventually crystallized. All the products were purified by crystallizing from EtOAc–petroleum ether.

5-Bromo-2-[(diphenylmethyl)amino]pyrimidine (13). After 2-[(diphenylmethyl)amino]pyrimidine (10 g, 0.038 mol) was dissolved in 50 ml of acetic acid at room temperature, bromine in acetic acid was added dropwise until the bromine color persisted; the mixture was added to 500 ml of water. The insoluble product was collected and recrystallized from EtOAc, mp 167°, yield 2.2 g (17%).

The nmr signal in dimethyl sulfoxide solution for the methyl proton of the diphenylmethyl group is a doublet with peaks at 6.3 and 6.45 ppm. The signal for the 4 and 6 protons of the pyrimidine ring is a singlet at 8.24 ppm, which indicates the 5 proton has been substituted by bromine.

Anal. Calcd for $C_{17}H_{14}BrN_3$: C, 60.01; H, 4.14. Found: C, 60.17; H, 4.25.

2-Amino-5-xanthen-9-ylpyrimidine (14). 2-Aminopyrimidine (0.1 mol, 9.5 g) and xanthen-9-ol (0.1 mol, 19.8 g) were added to 80 ml of glacial acetic acid and heated to refluxing temperature for 18 hr. The solution was added to 400 ml of water. The insoluble material was shown to be a mixture. It was separated on a chromatographic column of 1 kg of Grace silica gel, grade 950, with $CHCl_3$ and yielded 4.3 g (15%) of **14**, mp 213°.

Anal. Calcd for $C_{17}H_{13}N_3O$: C, 74.16; H, 4.73; N, 15.26. Found: C, 74.12; H, 4.87; N, 15.26.

The substitution reaction was slow enough to allow xanthen-9-ol to be partially oxidized to xanthen-9-one. Both xanthen-9-one and unreacted 2-aminopyrimidine were isolated from this chromatography.

2-Amino-5-(5*H*-dibenzo[*a*,*d*]cyclohepten-5-yl)pyrimidine (15). 2-Aminopyrimidine (0.1 mol, 9.5 g) and 5*H*-dibenzo[*a*,*d*]cyclohepten-5-ol (0.1 mol, 20.8 g) were dissolved in 100 ml of glacial acetic acid and heated under reflux for 28 hr. The mixture was poured into water, and the solid was collected by filtration. The product was crystallized from alcohol, yield 16.3 g (57%), mp 241°.

Anal. Calcd for $C_{19}H_{15}N_3$: C, 79.97; H, 5.30. Found: C, 80.00; H, 5.40.

2-(10,11-Dihydro-5*H*-dibenzo[*a*,*d*]cyclohepta-1,4-dien-5-ylamino)pyrimidine (6) and N^2,5-Bis(10,11-dihydro-5*H*-dibenzo[*a*,*d*]cyclohepta-1,4-dien-5-yl)-2-aminopyrimidine (16). 10,11-Dihydro-5*H*-dibenzo[*a*,*d*]cyclohepta-1,4-dien-5-ol (0.2 mol) and 2-aminopyrimidine (0.2 mol) were dissolved in 200 ml of glacial acetic acid and heated to refluxing temperature for 64 hr. The cooled mixture was added to water, and the insoluble solid was collected. Tlc showed the crude solid to be a mixture of two compounds. These were characterized by nmr as compound **6** (80%) and compound **16** (20%). The crude mixture was developed on a silica gel column ($CHCl_3$) to yield **16** (8.4%), mp 146° (crystallized from EtOAc).

Anal. Calcd for $C_{34}H_{29}N_3$: C, 85.14; H, 6.10; N, 8.76. Found: C, 85.14; H, 6.36; N, 8.75.

When the above reaction was repeated with a 20% excess of 2-aminopyrimidine, the precipitated solid yielded only compound **6** (Table I) (EtOAc).

4,6-Bis[(diphenylmethyl)amino]pyrimidine (17). 4,6-Diaminopyrimidine (0.1 mol) and benzhydrol (0.1 mol) were added to 150 ml of glacial acetic acid, heated to refluxing temperature for 24 hr, cooled, and added to water. The oil partly crystallized after standing for several days in fresh water. The solid was collected on a suction funnel and recrystallized from EtOAc, yield 2.1 g (9.6% based on the benzhydrol), mp 234°.

Anal. Calcd for $C_{30}H_{26}N_4$: C, 81.41; H, 5.92; N, 12.66. Found: C, 81.24; H, 5.91; N, 12.89.

4,6-Diamino-5-xanthen-9-ylpyrimidine (18). A solution of xanthen-9-ol (19.8 g, 0.1 mol) and 4,6-diaminopyrimidine (11 g, 0.1 mol) in 150 ml of glacial acetic acid was heated to refluxing temperature for 24 hr, then cooled and poured into cold water. The solid product was collected, and a sample was developed on tlc with EtOAc. Only one spot was evident after exposure to iodine vapor. The product was recrystallized from EtOH, mp 288° dec, yield 61%.

Anal. Calcd for $C_{17}H_{14}N_4O$: C, 70.33; H, 4.86; N, 19.30. Found: C, 70.62; H, 4.55; N, 19.05.

2-Amino-6-chloro-5-(diphenylymethyl)-4-hydroxypyrimidine (19). 2-Amino-4,6-dichloropyrimidine (0.1 mol, 16.4 g) and benzhydrol (0.1 mol, 18.4 g) were dissolved in 80 ml of glacial acetic acid, heated to refluxing temperature for 24 hr, and poured into 400 ml of water. The solid product was crystallized from EtOAc–petroleum ether and yielded 7.1 g (46%), mp 253°.

Anal. Calcd for $C_{17}H_{14}ClN_3O$: C, 65.48; H, 4.52; N, 13.47; Cl, 11.37. Found: C, 65.27; H, 4.69; N, 13.20; Cl, 11.42.

2-Amino-6-chloro-5-(diphenylmethyl)-4-hydroxypyrimidine was prepared in a similar manner from 2-amino-6-chloro-4-hydroxypyrimidine and benzyhydrol, mp 254°, yield 25%.

2-Amino-6-chloro-4-hydroxy-5[(2-methoxydiphenyl)methyl]-pyrimidine (20). 2-Amino-4,6-dichloropyrimidine (0.1 mol, 16.4 g) and 2-methoxybenzhydrol (0.1 mol, 21.4 g) were reacted in the manner described for the preparation of **19**, yield 14%, mp 255–256°.

Anal. Calcd for $C_{18}H_{16}ClN_3O_2$: C, 63.24; H, 4.21; N, 12.29; Cl, 10.37. Found: C, 63.23; H, 4.83; N, 12.07; Cl, 10.38.

6-Chloro-5-(diphenylmethyl)-2,4-dihydroxypyrimidine (21). To a cooled solution (20% of 2-amino-6-chloro-5-(diphenylmethyl)-4-hydroxypyrimidine (0.08 mol, 25.0 g) in a minimum amount of glacial acetic acid, was added, gradually, sodium nitrite (0.17 mol, 11.72 g), and the solution was stirred for 18 hr. One liter of water was added to the solution. The product was collected and crystallized from EtOAc–petroleum ether, mp 238°, yield 15.7 g (62.19%).

Anal. Calcd for $C_{17}H_{13}ClN_2O_2$: C, 65.28; H, 4.18; N, 8.97; Cl, 11.33. Found: C, 65.45; H, 4.22; N, 9.05; Cl, 11.26.

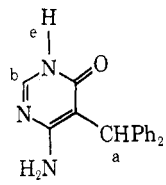
6-Amino-5-(diphenylmethyl)-2,4-dihydroxypyrimidine (22) and 2,4-Diamino-5-(diphenylmethyl)-6-hydroxypyrimidine (23). 6-Chloro-5-(diphenylmethyl)-2,4-dihydroxypyrimidine (0.02 mol. 7.0 g) was dissolved in excess alcoholic ammonia and heated at 150° for 12 hr in a bomb. The solution was evaporated. The resulting solid was shown by nmr to be a mixture of 6-amino-5-(diphenylmethyl)-2,4-dihydroxypyrimidine (30%) and 2,4-diamino-5-(diphenylmethyl)-6-hydroxypyrimidine (70%). The latter was separated from the mixture by crystallization from EtOAc, mp 248°, with characteristic nmr signals as presented in Table III. This compound (**23**) had an nmr signal, in deuterated chloroform, identical with the nmr signal of 2,4-diamino-5-(diphenylmethyl)-6-hydroxypyrimidine in deuterated chloroform. Compound **23** gave a mass ion of 292 (calculated 292) as determined on the Varian Mat 731 mass spectrometer.

6-Amino-5-(diphenylmethyl)-2,4-dihydroxypyrimidine was also isolated with good recovery of the amount indicated by the spectrum, mp 324°.

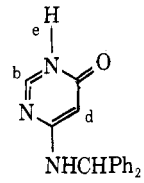
Anal. Calcd for $C_{17}H_{15}N_3O_2$: C, 69.91; H, 5.15; N, 14.32. Found: C, 69.70; H, 5.27; N, 14.20.

4-Amino-5-(diphenylmethyl)-6-hydroxypyrimidine (24) and 4-(Diphenylmethyl)amino-6-hydroxypyrimidine (25). 4-Amino-6-chloropyrimidine (0.1 mol, 13 g) and benzhydrol (18.4 g) were

added to 80 ml of glacial acetic acid and heated under reflux for 16 hr. The product was precipitated with water and was crystallized from dilute alcohol. The C, H, and N analyses were correct for $C_{17}H_{15}N_3O$, but the nmr spectra indicated a 50:50 mixture of 4-amino-5-(diphenylmethyl)-6-hydroxypyrimidine and 4-[(diphenylmethyl)amino]-6-hydroxypyrimidine. The mixture was separated on a silica gel column with $CHCl_3$. Each compound was characterized by its nmr taken in dimethyl sulfoxide; the assignments are shown below.



δ, ppm
a, 5.66
b, 7.82
c, 5.97
e, 11.75



δ, ppm
a, 6.03
b, 7.87
c, 7.80
d, 5.22
e, 11.75

4-Amino-6-hydroxy-5-[2-methoxy(diphenylmethyl)]pyrimidine (26). 4-Amino-6-chloropyrimidine (0.1 mol, 13.0 g) and 2-methoxybenzhydrol (0.1 mol, 21.4 g) were added to 80 ml of acetic acid and heated under reflux for 16 hr. The product was precipitated by adding the mixture to 400 ml of water. It was purified by crystallization from EtOAc–petroleum ether, yield 14 g (43%), mp 293° dec.

Anal. Calcd for $C_{18}H_{17}N_3O_2$: C, 70.34; H, 5.58; N, 13.67. Found: C, 70.29; H, 5.81; N, 13.88.

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Registry No.—**1**, 50259-14-8; **2**, 50259-15-9; **3**, 50259-16-0; **4**, 50259-17-1; , 50259-18-2; **6**, 50259-19-3; **7**, 50259-20-6; **8**, 50259-21-7; **9**, 50259-22-8; **10**, 50259-23-9; **11**, 50259-24-0; **12**, 50430-99-4; **13**, 50259-25-1; **14**, 50259-26-2; **15**, 50259-27-3; **16**, 50259-28-4; **17**, 50259-29-5; **18**, 50431-00-0; **19**, 50259-30-8; **20**, 50259-31-9; **21**, 50259-32-0; **22**, 50259-33-1; **23**, 50259-34-2; **24**, 50259-35-3; **25**, 50259-36-4; **26**, 50259-37-5; 2-aminopyrimidine, 109-12-6; 2-amino-4,6-dimethylpyrimidine, 767-15-7; 4,6-diaminopyrimidine, 2434-56-2; 2-amino-4,6-dichloropyrimidine, 56-05-3; 2-amino-6-chloro-5-(diphenylmethyl)-4-hydroxypyrimidine, 50259-38-6; 6-chloro-5-(diphenylmethyl)-2,4-dihydroxypyrimidine, 50259-39-7; 4-amino-6-chloropyrimidine, 5305-59-9.

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Dimetalated Heterocycles as Synthetic Intermediates. V. Dianions Derived from Certain 2-Hydroxy-4-methylpyrimidines, 2-Amino-4-methylpyrimidines, and Related Compounds†[1]

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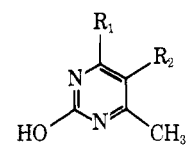
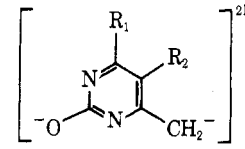
A convenient new method, involving dianion intermediates, has been developed for side-chain elaboration of 2-hydroxy-4-methylpyrimidines (**1a–c**), 2-anilino-4-methyl-6-phenylpyrimidine (**15a**), 2-amino-4-methylpyrimidine (**15b**), and 2-methyl-4(3*H*)-quinazolinone. The dianions, prepared by twofold metalation of the parent heterocycles with *n*-butyllithium in THF–hexane or sodium amide in liquid ammonia, reacted with benzyl chloride and carbonyl compounds to selectively establish exocyclic carbon–carbon bonds. Reaction of 4-hydroxy-2,6-dimethylpyrimidine (**8**) with 2 equiv of *n*-butyllithium produced a mixture of isomeric dianions (**9a–b**) in which **9a**, resulting from abstraction of a proton from the 4-methyl position, predominated.

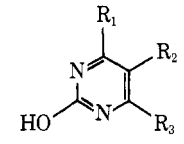
Although certain 2-hydroxy-, 2,4-dihydroxy-, 2-amino-, and 2,4-diaminopyrimidines containing a nuclear methyl substituent have been reported to undergo active hydrogen reactions such as aldol and Claisen condensations,[2] such processes generally appear to involve only low, equilibrium-controlled concentrations of carbanionic species. Recently, Klein and Fox[3] have used the Wittig reaction of phosphonium salt **4** with several aldehydes for the synthesis of 6-substituted uracils. We now describe a simple new method for elaboration of the methyl group of 2-hydroxypyrimidines (**1**) which avoids the necessity for hydroxyl masking or the preparation of phosphonium salts such as **4**. The procedure is based on initial generation of dianions (**2**), followed by treatment with various electrophilic reagents to form the appropriate C-substituted derivatives (**3**). Dianions derived from pyrimidines possessing other arrangements of hydroxyl and methyl, as well as those having suitably positioned mercapto and methyl, anilino and methyl, or amino and methyl groups, can be formed and utilized in a similar fashion.



1a, $R_1 = CH_3$; $R_2 = C_6H_5$
b, $R_1 = C_6H_5$; $R_2 = H$
c, $R_1 = CH_3$; $R_2 = H$



2a, $R_1 = CH_3$; $R_2 = C_6H_5$
b, $R_1 = C_6H_5$; $R_2 = H$
c, $R_1 = CH_3$; $R_2 = H$
d, $R_1 = C_6H_5(CH_2)_2$; $R_2 = C_6H_5$



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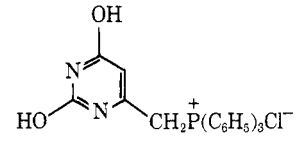

4

Results and Discussion

In an initial search for suitable basic reagents, the readily available 2-hydroxy-4,6-dimethyl-5-phenylpyrimidine