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Reaction of Pyrimidines with Diarylmethyl Cations

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Pyrimidine is not alkylated by diarylmethyl cations, but substitutions do occur at an endocyclic nitrogen with 2- and 4-hydroxypyrimidine and at the sulfur of 2-mercaptopyrimidine. Diarylmethylations occur exclusively at the 5-carbon position of 2,4-dihydroxy-, 2,4,6-trihydroxy-, and 6-amino-2,4-dihydroxypyrimidines. The effects of Lewis acid catalysts as well as substituents on the diarylmethyl cations on the alkylation reactions are discussed. Also, alternate synthetic routes to the 5-diarylmethylpyrimidines are given.

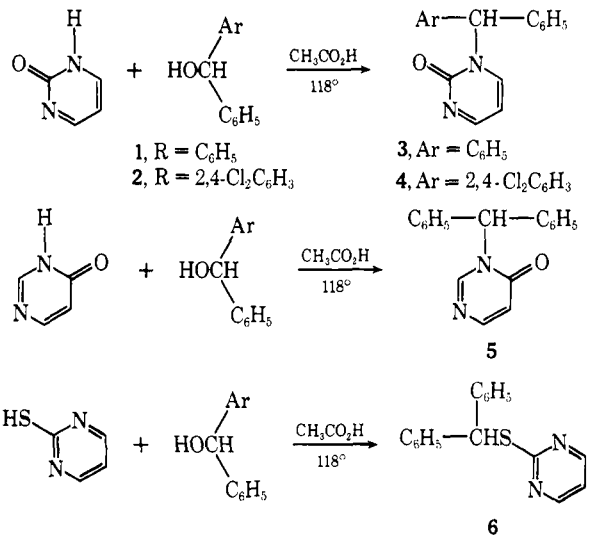
Pyrimidine and pyrimidine derivatives present several electron-rich nucleophilic centers where a carbonium ion may attack. Only one example of this reaction is reported with a diarylmethyl cation, and in this case the extranuclear nitrogen of 2-aminopyrimidine is alkylated.[1] On the other hand, alkylations of a carbon atom are reported for 2-hydroxypyridine,[2] thiophene,[3] 9-methylcarbazole,[4] pyrrole,[5] hydroxyquinolines,[6] and indoles.[7] The 2-, 4-, and 6-carbon atoms in pyrimidine are electron deficient by virtue of the electron-withdrawing effect of the nitrogen atoms and are not susceptible to alkylation.[8] Carbonium ion alkylations, therefore, could be expected to take place only at an electron-rich ring nitrogen or perhaps at the 5-carbon atom, although the latter is made slightly electron deficient by the general inductive effect. This report describes the reactions of diarylmethyl carbonium ions with pyrimidine, mercaptopyrimidine, and hydroxypyrimidines.

Results

No C or N alkylation products of pyrimidine were isolated when pyrimidine was treated with benzhydrol (1) in acetic acid either in the presence or absence of a Lewis acid catalyst. A very small amount of *N*-acetyl(diphenylmethyl)amine was isolated and the remaining 1 was recovered as diphenylmethyl acetate. The conversion of 1 to diphenylmethyl acetate was shown to occur quantitatively within 15 min in hot acetic acid.

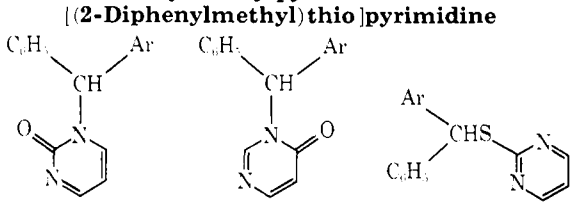
One electron-releasing substituent on pyrimidine, such as hydroxy or mercapto group in the 2 or 4 position, supplied sufficient electron density for electrophilic attack to take place at one of the heteroatoms (Scheme I). Partial alkylation of 2-hydroxypyrimidine occurred with 1 and with 2,4-dichlorobenzhydrol (2) in acetic acid to give low yields of the respective 1-diarylmethyl-2(1*H*)-pyrimidinones (3 and 4, Table I). Addition of boron trifluoride had little effect. More complete alkylation of 4-hydroxypyrimidine occurred with 1 to furnish 3-diphenylmethyl-4(3*H*)-pyrimidinone (5, Table I). The diphenylmethyl cation attacked the extranuclear sulfur of 2-mercaptopyrimidine to give a moderately good yield of [(2-diphenylmethyl)thio]pyrimidine (6, Table I).

Scheme I



Two or three electron-contributing groups at the 2, 4, and 6 positions of pyrimidine caused the diarylmethyl cations to be attracted to the 5 position of pyrimidine (Scheme II). Reaction of uracil or 2-thiouracil, however, did not occur with 1 after 5 days in refluxing acetic acid. When boron trifluoride or stannic chloride was added, the alkylation was complete in several hours and nearly quantitative yields of the 5-(diphenylmethyl) derivatives (7 and 8, Table II) were isolated. Similar reaction conditions with 1 and 6-methyluracil gave a good yield of 6-methyl-5-(diphenylmethyl)uracil (9, Table II). Chlorine substituents of 2 had only a slightly inhibitory effect on the carbonium ion alkylations of uracil and 6-methyluracil. Yields of the 5-[(2,4-dichloro)diphenylmethyl]uracils (10 and 11, Table II) were only a few per cent lower than the yields for the corresponding 5-(diphenylmethyl)uracils (7 and 8).

Table I
***N*-Diarylmethylpyrimidines and [(2-Diphenylmethyl)thio]pyrimidine**

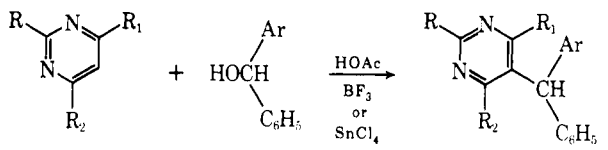


3, 4 5 6

Compd no.	Ar	Mp, °C	% yield
3	C_6H_5	204	13
4	$2,4\text{-}Cl_2C_6H_3$	185–187	18
5	C_6H_5	158–159	51
6	C_6H_5	104	63

However, the chloro substituents had a pronounced inhibitory effect upon the reactions with 4,6-dihydroxypyrimidine and 4,6-dihydroxy-2-(methylthio)pyrimidine. A 40% yield of 5-[(2,4-dichloro)diphenylmethyl]uracil (**12**, Table II) was obtained from **2** and 4,6-dihydroxypyrimidine, compared with a 78% yield of 4,6-dihydroxy-5-(diphenylmethyl)pyrimidine (**13**, Table II) obtained from **1** and 4,6-dihydroxypyrimidine. A very low yield of 5-[(2,4-dichloro)diphenylmethyl]-4,6-dihydroxy-2-(methylthio)pyrimidine (**14**, Table II) resulted from 4,6-dihydroxy-2-(methylthio)pyrimidine and **2** while the similar 4,6-dihydroxy-2-methylpyrimidine reacted quantitatively with **1** to give 4,6-dihydroxy-5-(diphenylmethyl)-2-methylpyrimidine (**15**, Table II).

Scheme II

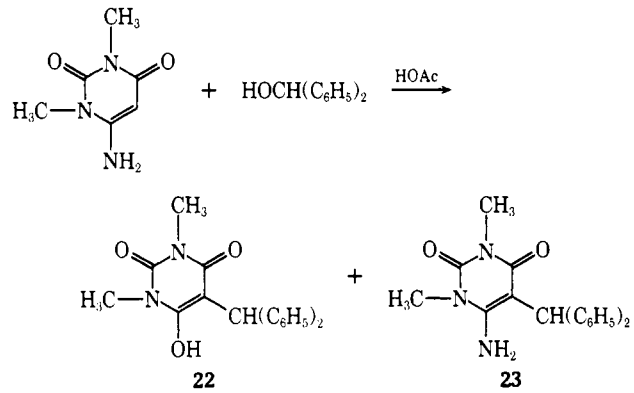


Barbituric acid was alkylated by diarylmethyl cations without the aid of strong acid catalysts, but the yields were low (Table II), even with longer than usual reaction times. When either stannic chloride or boron trifluoride was present, alkylation with **1**, 4-chlorobenzhydrol, or **2** gave good to excellent yields of the respective 5-diarylmethylbarbituric acids (**16**, **17**, and **18**). The alkoxy groups of 3,4-diethoxybenzhydrol retarded the alkylation reaction of barbituric acid (**19**, Table II), but this effect was less than that observed with the 2,4-dichloro- and 4-chlorobenzhydrols. Tritylation of barbituric acid was accomplished, but because of an unusual and interesting behavior of the product the results will be reported in another paper.

A Lewis acid catalyst did not enhance the diphenylmethylation of 6-aminouracil. The yield of 6-amino-5-(diphenylmethyl)uracil (**20**, Table II) obtained without the catalyst was twice that with the catalyst. Alkylations of hydroxypyrimidines by diphenylmethyl cation were attempted in concentrated sulfuric acid and in polyphosphoric acid; both were unsuccessful because of low yields. Sulfuric acid, added to the acetic acid solution, may have catalyzed the reaction of **1** with 4-amino-6-hydroxy-2-pyrimidinethiol to give a 52% yield of 4-amino-6-hydroxy-5-(diphenylmethyl)-2-pyrimidinethiol (**21**, Table II).

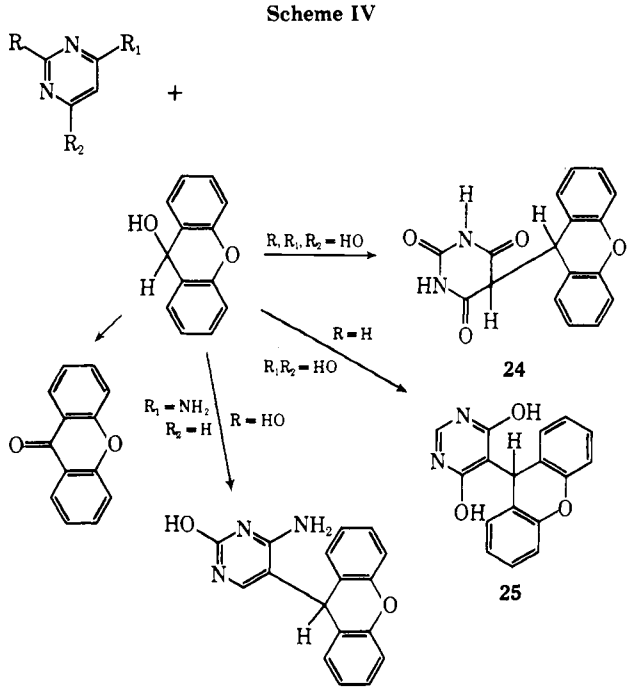
A Lewis acid catalyst was not required for the reaction between **1** and 6-amino-1,3-dimethyluracil. Alkylation at the 5-carbon position was at least 80% complete in hot acetic acid. Partial hydrolysis of the 6-amino group occurred and the reaction mixture yielded the major product 1,3-dimethyl-5-(diphenylmethyl)barbituric acid (**22**) and the minor product 6-amino-1,3-dimethyl-5-(diphenylmethyl)uracil (**23**, Scheme III).

Scheme III



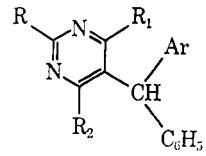
Xanthen-9-ol is completely oxidized to xanthen-9-one within 15 min in hot acetic acid. Successful competitive alkylations of pyrimidines by xanthen-9-ol occurred rapidly or otherwise not at all. Barbituric acid and 4,6-dihydroxypyrimidine gave excellent yields of the corresponding 5-(9-xanthenyl)pyrimidines (**24** and **25**, Table III). Attempted reactions with uracil and thiouracil, on the other hand, failed because of their low solubility in acetic acid. Cytosine gave a 55% yield of 5-(9-xanthenyl)cytosine (**26**, Table III), but only a very low yield of 4-amino-5-(diphenylmethyl)-2-hydroxypyrimidine (**27**, Table II) was obtained from cytosine and **1**.

Scheme IV



Since fluoren-9-ol was oxidized in acetic acid, reactions of this tricyclic carbinol with hydroxypyrimidines were not attempted. The reaction of 10,11-dihydro-5*H*-dibenzo[*a*,*d*]cyclohepten-5-ol with uracil gave a moderately good yield of 5-(10,11-dihydro-5*H*-dibenzo[*a*,*d*] cyclohepten-5-yl)uracil (**28**, Table III) and with barbituric acid gave an excellent yield of 5-(10,11-dihydro-5*H*-dibenzo[*a*,*d*]cyclohepten-5-yl)barbituric acid (**29**, Table III). The large dibenzo[*a*,*d*]cycloheptene group of **29** is restricted from freely rotating about the bond to the pyrimidine ring. The nmr doublet signal, centered at 3.85 ppm from the pyrimidyl-5 proton, and the doublet, centered at 4.50

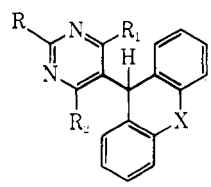
Table II
5-Diarylmethylhydroxypyrimidines and 5-Diarylmethyl Mercaptopyrimidines



No.	R	R_1	R_2	Ar	Mp, °C	% yield
7	HO	HO	H	C_6H_5	298–300	96[a]
8	HS	HO	H	C_6H_5	264	99
9	HO	HO	CH_3	C_6H_5	285–287	80[b]
10	HO	HO	H	2,4-$Cl_2C_6H_3$	294	81,[a] 95[b]
11	HO	HO	CH_3	2,4-$Cl_2C_6H_3$	247–249	71[b]
12	H	HO	HO	2,4-$Cl_2C_6H_3$	305	40
13	H	HO	HO	C_6H_5	329–330	78
14	CH_3S	HO	HO	2,4-$Cl_2C_6H_3$	255	14
15	CH_3	HO	HO	C_6H_5	>300	98
16	HO	HO	HO	C_6H_5	220	98[b,c]
17	HO	HO	HO	4-ClC_6H_4	110[d]	73[e]
18	HO	HO	HO	2,4-$Cl_2C_6H_3$	234	67,[a,f] 83[b]
19	HO	HO	HO	3,4-$(C_2H_5O)_2C_6H_3$	180–182	42
20	HO	HO	NH_2	C_6H_5	330–342	67[g]
21	HS	NH_2	OH	C_6H_5	170–180[d]	52
27	HO	NH_2	H	C_6H_5	236	4[h]

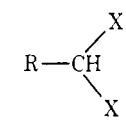
[a] $SnCl_4$ was used as catalyst (5 g/0.1 mol). [b] With BF_3 catalyst (5 g/0.1 mol). [c] The yield was 56% without BF_3 catalyst. [d] Solvated. [e] The yield was 37.5% without BF_3. [f] The yield was 22% without catalyst. [g] The yield was 38.5% with $SnCl_4$ catalyst. [h] The same reaction conditions were used for compound **21**.

Table III
5-(9-Xanthenyl)- and 5-(10,11-Dihydro-5*H*-dibenzo[*a*,*d*]cyclohepten-5-yl)pyrimidines



Compd no.	X	R	R_1	R_2	Mp, °C	% yield
24	O	HO	HO	HO	290	81
25	O	H	HO	HO	285	95
26	O	HO	H_2N	H	320 dec	55
28	$(CH_2)_2$	HO	HO	H	295	68
29	$(CH_2)_2$	HO	HO	HO	244–246	85

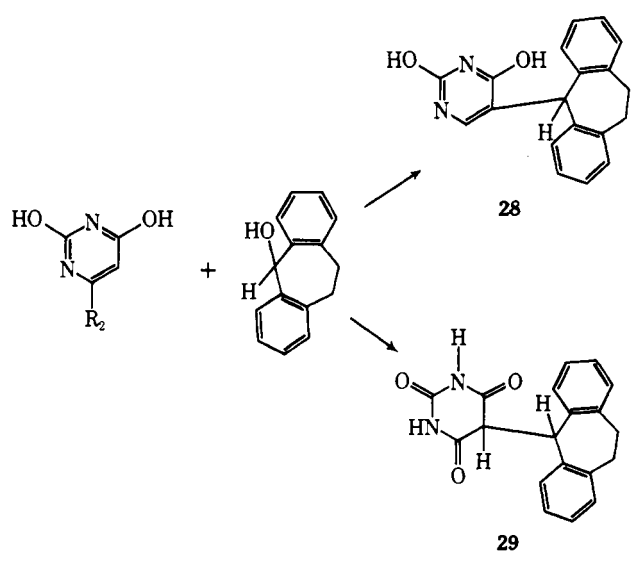
Table IV
Aralkyl Malononitriles and Malondiamides



Compd no.	R	X	Mp, °C	% yield
30	$(C_6H_5)_2CH$	$CONH_2$	285	91.2
31	2,4-$Cl_2C_6H_3CHC_6H_5$	$CONH_2$	270–274	55.6[a]
32	$(C_6H_5)_2CH$	C≡N	62–64	87
33	2,4-$Cl_2C_6H_3CHC_6H_5$	C≡N	108–114	85
34	$C_{13}H_9O$[b]	C≡N	184	75
35	$(C_6H_5)_3C$	C≡N	155	45.5

[a] The yield was reduced to 47.4% when glacial acetic acid was used as the reaction solvent. [b] Xanthen-9-yl.

Scheme V



ppm from the 9,10-dihydrobenzo[*a*,*d*]cycloheptenyl-5 proton, have *J* values of 9 Hz indicating that the molecule exists approximately two-thirds of the time in the trans configuration. Rotation of the xanthen-9-ol group bonded to the 5 position of barbituric acid, as in **25**, is not restricted and the signals from the vicinal protons at the bond are split by only 3 Hz.

An alternate synthesis of 5-diarylmethylpyrimidines was investigated wherein malonic acid derivatives were alkylated by arylmethyl cations, and the products were cyclized. Malononitrile failed to react with either **1** or **2** in hot acetic acid and, when boron trifluoride was added, exothermic reactions occurred to give intractable mixtures of products. However, the two carbinols did react with malondiamide in acetic acid and boron trifluoride (Scheme VI) but gave low yields of the diarylmethylmalondiamides (**30** and **31**, Table IV). Yields improved when the solvent was formic acid and a nearly quantitative yield of diphenylmethylmalondiamide (**30**) was obtained. The halogen substituents of **2**, here again, retarded the carbonium ion reaction and a lower yield of 2,4-dichloro(diphenylmethyl)malondiamide (**31**) resulted. The malondiamides (**30** and **31**) were dehydrated with phosphorus oxychloride in acetamide to give good yields of the corresponding diarylmethylmalononitriles (**32** and **33**, Table IV). The reactions of xanthen-9-ol and triphenyl-

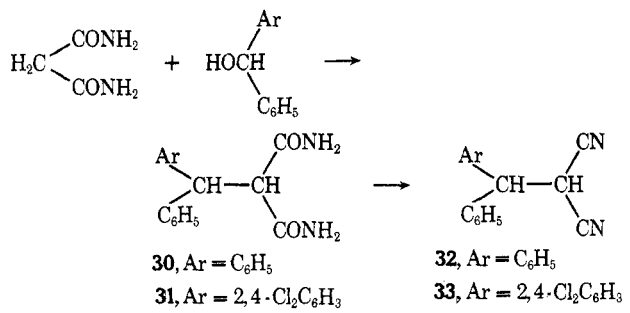
Table V
Cyclizations of 2-Diarylmethylmalondiamides (Compounds 12 and 13)

Base	$HCONH_2$, ml	$(CH_3)_2SO$, ml	Temp, °C	Time, hr	% yield of pyrimidine	% recovery of diamide
$KOC(CH_3)_3$	150	0	Reflux	3	<2[a]	*ca.* 90
$NaOC_2H_5$	50	d	Reflux	10	0[a]	*ca.* 100
$KOC(CH_3)_3$	50	50	100	15	46.8[a]	26
$NaOCH_3$	50	50	100	15	38.8[a]	52
$NaOCH_3$	40	60	135	16	53.2[a]	25
$NaOCH_3$[b]	50	50	125	15	78[a]	17
$NaOCH_3$	50	50	125	15	60.5[c]	25
NaOH	50	50	125	7	8.6[c]	75

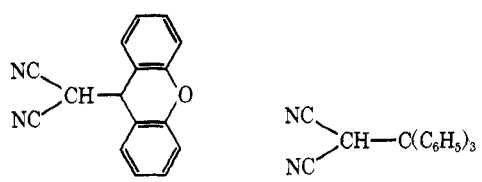
[a] Results for 4,6-dihydroxy-5-(diphenylmethyl)pyrimidine. [b] After the initial addition of 2.2 equiv (6 g) of $NaOCH_3$, 2 g was added at 2- and 4-hr intervals. [c] Results for 5-[(2,4-dichloro)diphenylmethyl]-4,6-dihydroxypyrimidine.

methanol with malononitrile in acetic acid were uncomplicated and gave good yields of the arylmethylmalononitriles (**34** and **35**, Table IV).

Scheme VI



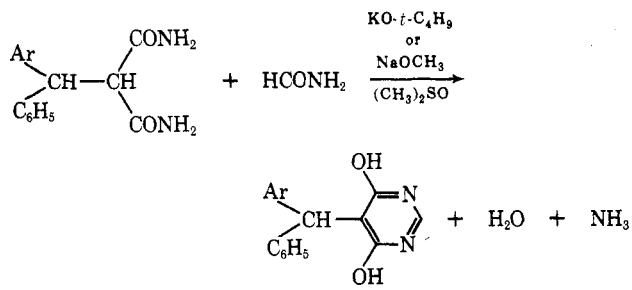
30, Ar = C_6H_5
31, Ar = 2,4-$Cl_2C_6H_3$
32, Ar = C_6H_5
33, Ar = 2,4-$Cl_2C_6H_3$



34 **35**

The malondiamides (**30** and **31**) failed to cyclize when heated neat with formamide, with formamide in formic acid, or with formamide and formic acid in dimethylformamide. Cyclization also failed with formamide in acetic acid, in sulfuric acid, or in polyphosphoric acid. Only small yields of the desired pyrimidines (**12** and **13**, Table V) were obtained when formamide was heated with **30** and **31** in alcohol in the presence of sodium methylate. The most complete cyclizations (Scheme VII) were accomplished in dimethyl sulfoxide solution with formamide and 2.2 mol equiv or more of either potassium *tert*-butoxide or sodium methoxide (Table V).

Scheme VII



12, Ar = C_6H_5
13, Ar = 2,4-$Cl_2C_6H_3$

The 5-diarylmethyluracils **10** and **7** were converted to the corresponding 2,4-dichloropyrimidines and the halogens on the pyrimidine ring were selectively and quantitatively removed by catalytic reduction[9] to give 5-diarylmethylpyrimidines.

Experimental[10] Section

1-Diarylmethyl-2(1*H*)-pyrimidones (3 and 4), 3-(Diphenylmethyl)-4(3*H*)-pyrimidinone (5), and 2-[(Diphenylmethyl)thio]pyrimidine (6) (Table I). 2-Hydroxy-, 4-hydroxy-, and 2-thiopyrimidines (0.1 mol) were heated separately with 0.1 mol of the appropriate diarylcarbinol in 50–100 ml of glacial acetic acid for 5–8 hr in the absence of a catalyst. The solid products, obtained by pouring the cooled solution into water, were crystallized from mixtures of benzene–petroleum ether, ethyl acetate–petroleum ether, and dilute alcohol.

This same procedure was repeated with 2-hydroxyprimidine and benzhydrol with 5.0 g of boron trifluoride etherate. The yield was increased by 2%.

5-Diarylmethyluracils (7–11) (Table II). Uracil, 2-thiouracil, or 6-methyluracil (0.1 to 0.80 mol) and an equal molar quantity of the appropriate diarylcarbinol were added to glacial acetic acid (100 ml for each 0.1 mol of the uracil). Five grams of boron trifluoride etherate or 3–5 g of $SnCl_4$ was added for each 0.1 mol of the uracil. The mixture was heated at refluxing temperature until the reaction was complete, usually about 5 hr. The reaction end point was determined by periodically withdrawing and inspecting samples. The product precipitated and crystallized when a sample of a completed reaction solution was added to cold water. Oily mixtures, containing some diarylcarbinol acetate, were obtained from incomplete reaction mixtures. The completed reaction solution was cooled and poured into cold water. The solid product was collected by filtration, washed several times with water, and crystallized from alcohol–water mixtures.

The above procedure was repeated with uracil, with the exception that diphenylmethyl bromide was substituted for the diarylcarbinol. The yield of compound **7** was 74%.

5-Diarylmethyl-4,6-dihydroxypyrimidines (12–15) (Table II). 4,6-Dihydroxypyrimidine, 4,6-dihydroxy-2-(methylthio)pyrimidine, or 4,6-dihydroxy-2-methylpyrimidine (0.1 mol) and benzhydrol or 2,4-dichlorobenzhydrol (0.1 mol) were added to 100 ml of glacial acetic acid. $SnCl_4$ (2–6 g) was added and the mixture was heated at refluxing temperature for 4–5 hr. The cooled reaction mixtures were poured into cold water. The precipitated products were collected and crystallized from alcohol.

5-Diarylmethylbarbituric Acids (16–19) (Table II). Barbituric acid (12.7 g or 0.1 mol) and the appropriate diarylcarbinol (0.1 mol), boron trifluoride etherate (5 g) or $SnCl_4$ (3 g), in 100–200 ml of glacial acetic acid were heated at refluxing temperature for 2–5 hr. The reaction time was 2–5 days when the Lewis acid catalyst was not used. The products were isolated and purified in the manner described in the previous paragraph.

6-Amino-5-(diphenylmethyl)uracil (20) (Table II). Two mixtures were prepared, consisting of 0.1 mol (12.7 g) of 6-aminouracil and 0.1 mol (18.4 g) of benzhydrol in 100 ml of glacial acetic acid. Four grams of $SnCl_4$ was added to one mixture. Each mixture was heated at refluxing temperature for 24 hr. The product was isolated in the manner described in a previous paragraph.

4-Amino-5-(diphenylmethyl)-6-hydroxy-2-pyrimidinethiol (21) (Table II). Benzhydrol (19.8 g or 0.1 mol), 4-amino-6-hydroxy-2-pyrimidinethiol (14.2 g of 0.1 mol), and 1 ml of concentrated H_2SO_4 were added to 100 ml of glacial acetic acid. The mixture was heated at refluxing temperature for 6 hr, then cooled and added to water. The product was collected and crystallized from benzene, ethyl acetate, and alcohol.

5-Diphenylmethyl-1,3-dimethylbarbituric Acid and 6-

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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(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