TABLE VI

PHYSICAL AND ANALYTICAL DATA OF DIAZEPINES

Diazepine	Yield, %[a]	Physical state[b]	$n^{25}D$ or mp, °C	Molecular formula	Analysis,[c] % Calcd C	Calcd H	Calcd N	Found C	Found H	Found N
3a	97	Red oil	1.5400	$C_8H_{10}N_2O_2$	57.82	6.07	16.86	57.40	5.93	16.44
3b	84	Yellow oil	1.5276	$C_9H_{12}N_2O_2$	59.99	6.71	15.55	60.05	6.96	15.38
3c	98	Pale yellow needles[d]	55.5–56	$C_9H_{12}N_2O_2$	59.99	6.71	15.55	59.74	6.93	15.59
3d	41	Yellow oil	1.5065	$C_{10}H_{14}N_2O_2$	61.84	7.27	14.42	61.44	7.26	14.20
3e	72	Yellow oil	1.5140	$C_{10}H_{14}N_2O_2$	61.84	7.27	14.42	61.50	7.33	14.20
3f	65	Yellow needles[e]	90–91	$C_{10}H_{15}N_3O_2$	57.40	7.23	20.08	57.05	7.20	19.80
5a	64	Orange needles[c]	52–54	$C_{12}H_{10}N_2O$	72.71	5.08	14.13	72.71	5.23	14.00
5b	61	Pale yellow crystals[f]	173–175 dec	$C_{12}H_{12}N_2O_2S$[g]	58.06	4.87	11.28	58.37	4.77	11.06

[a] After chromatography. [b] Purification of the oily diazepines was achieved by short-path distillation at 45–60° (0.1–0.5 mm). [c] Owing to volatility and instability, analytical data on the oily compounds was difficult to obtain and the values given are the best of at least quadruplicate determinations. [d] From benzene–petroleum ether. [e] From ether–petroleum ether (bp 35–60°). [f] From benzene. [g] Calcd: S, 12.89. Found: S, 13.08.

Registry No.—**2a**, 23025-55-0; **2b**, 22928-83-2; **2b** picrate, 22928-84-3; **2c**, 22928-85-4; **2d**, 22928-87-6; **2e**, 23025-59-4; **2f**, 23025-60-7; **2g**, 23025-61-8; **3a**, 17377-08-1; **3b**, 22928-90-1; **3c**, 22928-91-2; **3d**, 22928-95-6; **3e**, 22928-97-8; **3f**, 23025-66-3; **4a**, 23031-08-5; **4b**, 23025-67-4; **5a**, 20169-43-1; **5b**, 23025-45-8; **7**, 20169-37-3; **8**, 20169-38-4; **10**, 22931-88-0.

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Synthesis of 4,5-Disubstituted Pyrimidines

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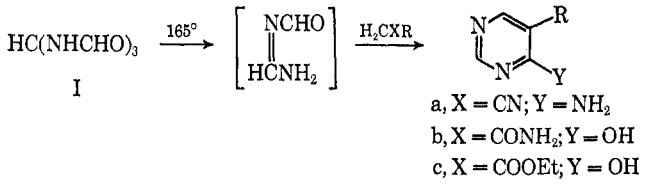
Several new 4-amino (or hydroxy) 5-substituted pyrimidines are prepared by the reaction of trisformylaminomethane with various substituted acetonitriles, acetamides, and corresponding esters, and the reaction results are discussed.

In a previous paper,[2] the synthesis of 4-amino (or hydroxy) 5-substituted pyrimidines by the reaction of trisformylaminomethane (I) with phenylacetonitriles (a) or *p*-nitrophenylacetamide (b) having an active methylene group was reported.



I

a, X = CN; Y = NH_2
b, X = $CONH_2$; Y = OH
c, X = COOEt; Y = OH

Pyrimidines of similar structure, with different substituent R, have been prepared by other workers.[3-7]

In this paper, the possibility of synthesis of 4-hydroxy-5-phenylpyrimidine from phenylacetamide, having a less active methylene group than *p*-nitrophenylacetamide, as well as the synthesis of 4-hydroxypyrimidines from the corresponding esters (c), were studied. Furthermore, in order to prepare new 4-amino (or hydroxy) 5-substituted pyrimidines and to extend the application of this synthetic method, substituted acetonitriles, acetamides, and the corresponding esters, with both electron-attracting and -releasing substituents, were used.

The reactions were carried out under the same conditions, using formamide as a solvent and *p*-toluenesulfonic acid as a catalyst.[8] However, the presence of formamide and the catalyst has been found to be unnecessary. The results of these reactions are presented in Table I.

Some 4-hydroxypyrimidines were also prepared by acid hydrolysis of the corresponding 4-aminopyrimidines. The results of the replacement reactions are summarized in Table II.

(1) Abstracted in part from the Ph.D. dissertation of A. H. K., University of Thessaloniki, Greece, 1967.
(2) G. Tsatsaronis and F. Effenberger, *Chem. Ber.*, **94**, 2876 (1961).
(3) H. Bredereck, G. Simchen, and H. Traut, *ibid.*, **98**, 3883 (1965).
(4) W. H. Davies and H. A. Piggot, *J. Chem. Soc.*, 347 (1945).
(5) W. H. Davies, A. W. Johnson, and H. A. Piggot, *ibid.*, 352 (1945).
(6) K. Huffman, F. Schaefer and G. Peters, *J. Org. Chem.*, **27**, 551 (1962).
(7) E. C. Taylor and J. G. Berger, *ibid.*, **32**, 2376 (1967).
(8) H. Bredereck, R. Gompper, and B. Geiger, *Chem. Ber.*, **93**, 1402 (1960).

TABLE I

SYNTHESES OF 4,5-DISUBSTITUTED PYRIMIDINES

Starting material RCH_2X		Reaction conditions	Product		Pure yield, %	Formula	Calcd, %			Found, %		
R	X		Compd	Y			C	H	N	C	H	N
α-$C_{10}H_7$	CN	A	II	NH_2	28	$C_{14}H_{11}N_3$	75.99	5.01	18.99	76.08	5.13	19.03
2-C_5H_4N	CN[a]	A	III	NH_2	54	$C_9H_8N_4$	62.77	4.68	32.54	62.73	4.54	31.99
3-C_5H_4N	CN[b]	A	IV	NH_2	52	$C_9H_8N_4$	62.77	4.68	32.54	62.51	4.60	32.28
4-C_5H_4N	CN[c]	A	V	NH_2	52	$C_9H_8N_4$	62.77	4.68	32.54	62.18	4.45	32.47
2-C_9H_6N	CN[d]	A[e]	VI	NH_2	38	$C_{13}H_{10}N_4$	70.25	4.54	25.21	69.71	4.48	25.36
4-C_9H_6N	CN[f]	A[e]	VII	NH_2	36	$C_{13}H_{10}N_4$	70.25	4.54	25.21	70.53	4.21	25.37
6-C_9H_6N	CN[g]	A[e]	VIII	NH_2	7	$C_{13}H_{10}N_4$	70.25	4.54	25.21	69.96	4.40	24.96
8-C_9H_6N	CN[h,i]	A[e]	IX	NH_2	10	$C_{13}H_{10}N_4$	70.25	4.54	25.21	70.13	4.49	25.15
CH_3	CN	A[j]	X	NH_2	1.8	$C_5H_7N_3$[k]	55.03	6.47	38.51	54.43	6.07	38.37
C_6H_5	$CONH_2$	A[l]	XI	OH	9	$C_{10}H_8N_2O$[m]	...	...	...	...	...	...
C_6H_5	COOEt	A[l]	XI	OH	0.3	$C_{10}H_8N_2O$	...	...	...	...	...	...
α-$C_{10}H_7$	$CONH_2$[n]	A	XII	OH	5	$C_{14}H_{10}N_2O$	75.65	4.54	12.61	75.36	4.25	12.60
α-$C_{10}H_7$	COOEt	A	No pyrimidine		...	...	...	...	...	...	...	...
3-C_5H_4N	$CONH_2$[o]	A	XIII	OH	25	$C_9H_7N_3O$	62.42	4.07	24.27	62.06	3.80	23.97
4-C_5H_4N	$CONH_2$[p]	A	XIV	OH	40	$C_9H_7N_3O$	62.42	4.07	24.27	62.50	3.82	24.40
p-$O_2NC_6H_4$	COOEt	A	XV	OH	40	$C_{10}H_7N_3O_3$[q]	...	...	...	...	...	...
C_9H_7	CN	A[r]	No pyridine		0.4	Bisformyl aminomethane						
C_6H_{13}	CN	A[s]	No pyrimidine		0.6	Bisformyl aminomethane						

[a] N. Sperber, *et al.*, *J. Amer. Chem. Soc.*, **73**, 5752 (1951). [b] Obtained from K & K Laboratories, Inc. [c] Prepared analogously to 2-pyridylacetonitrile, yield 58%. [d] W. Borsche and R. Manreuffel, *Chem. Abstr.*, **31**, 406 (1937); *Chem. Zentr.*, I, 2971 (1937). [e] Half quantities of reactants were used. [f] H. Lettré, *et al.*, *Chem. Ber.*, **85**, 397 (1952). [g] Prepared analogously to 2-pyridylacetonitrile from the 6-quinolylacetamide, yield 55%, mp 80–81°. [h] R. G. Jones, Q. F. Soper, O. K. Behrens, and J. W. Corse, *J. Amer. Chem. Soc.*, **70**, 2843 (1948). [i] B. Prijs, *et al.*, *Helv. Chim. Acta*, **37**, 90 (1954). [j] In a glass sealed tube heated in an autoclave. [k] R. R. Williams, A. E. Ruehle, and J. Finkelstein, *J. Amer. Chem. Soc.*, **59**, 526 (1937). [l] Without catalyst. [m] Reference 4. [n] W. Wenner, *Chem. Abstr.*, **44**, 9374c (1950). [o] A. Burger and C. Walter, *J. Amer. Chem. Soc.*, **72**, 1988 (1950). [p] A. Burger, *et al.*, *ibid.*, **74**, 3175 (1952). [q] Reference 2. [r] Fivefold quantities of reactants were used. [s] Tenfold quantities of reactants were used.

TABLE II

REPLACEMENTS OF THE SUBSTITUENT Y

Starting material			Product		Pure yield, %	Formula	Calcd, %			Found, %		
Compd	R	Y	Compd	Y			C	H	N	C	H	N
II	α-$C_{10}H_7$	NH_2	XII	OH	45	...	...	...	...	...	...	...
III	2-C_5H_4N	NH_2	XVI	OH	43	$C_9H_7N_3O$	62.42	4.07	24.27	62.13	3.90	24.13
IV	3-C_5H_4N	NH_2	XII	OH	50	...	...	...	...	...	...	...
XII	α-$C_{10}H_7$	OH	XVII	Cl	76	$C_{14}H_9N_2Cl$	69.82	3.77	11.63	69.42	3.40	11.77
XVII	α-$C_{10}H_7$	Cl	II	NH_2	54	...	...	...	...	...	...	...
XVII	α-$C_{10}H_7$	Cl	XVIII	$NHNH_2$	80	$C_{14}H_{12}N_4$	71.16	5.12	23.72	71.29	5.05	23.53

On the basis of the yields (Table I), it is found that the reactivity of RCH_2X, for the same substituent R, decreases in the order nitrile > amide > ester (X = CN, $CONH_2$, and COOEt, respectively). This is attributed to the higher electron-attracting effect of the CN group with respect to the $CONH_2$ and the COOEt group, with the result that the methylene group of nitrile becomes more active.

In addition, for the same substituent X, as the electron-attracting effect of the substituent R is increased, higher yields are obtained, provided that the hindrance effect of R is almost the same. This is evident from the reaction yields with α-naphthyl- and 4-quinolylacetonitrile, 3-pyridyl- and 4-pyridylacetamide, and phenyl- and *p*-nitrophenylacetic ethyl ester and from the reactions with propio-, valero-, and caprylonitrile, where R is an electron-releasing substituent. Thus no pyrimidine was obtained with valero- and caprylonitrile, although larger quantities of reactants were used to make possible the isolation of the expected pyrimidine, even in small amounts. However, from these reactions, bisformylaminomethane, in very small yield, was isolated. It was identified by mixture melting point and by comparison of the ir spectra with that of an authentic sample.[9] The mechanism of formation of bisformylaminomethane is under further investigation.

The yield also depends significantly on the steric bulk of the substituent R. Thus, in spite of the more electron-attracting effect, the yields with α-naphthyl- and 2-quinolylacetonitrile were, respectively, less than with phenyl- and 2-pyridylacetonitrile. The considerably smaller yield with 8-quinolyl- or 6-quinolylacetonitrile compared with α-naphthylacetonitrile is due to the formation of resinous by-products.

The ratio of the yields with amide and corresponding nitrile becomes greater as the electron-attracting effect

(9) C. W. Sauer and R. J. Bruni, *J. Amer. Chem. Soc.*, **77**, 2559 (1955).

of the substituent R increases. Thus for R = α-naphthyl, 3-pyridyl, and 4-pyridyl, the ratio of yields is increased, respectively. Consequently, for a more electron-attracting substituent R, the reaction yield with an amide would be expected to approach the yield with the corresponding nitrile. A similar increase of the ratio of yields with ester and corresponding amide is also observed.

The compound obtained by Novelli[10,11] by reaction of α-naphthylacetonitrile with formamide and described as α-naphthylmethyl-1,3,5-triazine was shown in this work to be the isomeric 4-amino-5-α-naphthylpyrimidine (II). The identification was based on mixture melting point and ir spectra. The aminopyrimidines showed the characteristic absorptions of the amino group[12-15] (1620–1670, 3100–3170, and 3288–3360 cm^{-1}).

Experimental Section

Melting points were taken on a Kofler hot-stage apparatus and are corrected. The melting point of 4-amino-5-methylpyrimidine (X) was obtained in a closed capillary tube because of its sublimation. All ir spectra were obtained as Nujol mulls on a Beckman IR-4 spectrophotometer.

Reaction Conditions (A, Table I).—A mixture of 0.05 mol of starting material (nitrile, amide, or ester), 14.5 g (0.1 mol) of trisformylaminomethane[16] (I), 8 ml (0.2 mol) of formamide, and 1 g of *p*-toluenesulfonic acid was heated with stirring for 7 hr at 170°.

4-Amino-5-α-naphthylpyrimidine (II).—The dark reaction mixture was acidified with 10% hydrochloric acid, diluted with water, treated with active carbon, and filtered, and the aminopyrimidine (II) was precipitated by basification with 8% sodium hydroxide and crystallized from benzene (charcoal). It is very soluble in chloroform and warm alcohol, and soluble in warm benzene and water. Recrystallizations from benzene (charcoal) gave white crystals, yield 3 g, mp 194–195°.

4-Amino-5-(pyridyl-2)-pyrimidine (III).—The reaction mixture was allowed to crystallize overnight. The product was filtered with suction, washed with a small amount of water, dried, and, after treatment with active carbon, crystallized from benzene, yield 4.9 g, mp 173–175°. From the filtrate, by basification, with 8% sodium hydroxide and extraction with benzene for 24 hr, an additional 0.5 g of III was obtained. Recrystallization from benzene (charcoal) gave white crystals, yield 4.7 g, mp 175–176°.

4-Amino-5-(pyridyl-3)-pyrimidine (IV).—In the same manner as above, white crystals of IV were obtained, yield 4.5 g, mp 196–197°.

4-Amino-5-(pyridyl-4)-pyrimidine (V).—As above, crude V was obtained, yield 5.4 g, mp 225–227°. Recrystallization from chloroform (charcoal) gave white crystals, yield 4.5 g, mp 228–229°.

4-Amino-5-(quinolyl-2)-pyrimidine (VI).—The reaction mixture was allowed to stand overnight. The crystalline product was separated and treated as in the case of II, giving, after crystallization from benzene (charcoal), crude VI, yield 2.9 g, mp 196–200°. Recrystallizations from benzene (charcoal) gave bright plates, yield 2.1 g, mp 201–201.5°.

4-Amino-5-(quinolyl-4)-pyrimidine (VII).—In the same manner as previously, crude VII was obtained, yield 2.5 g, mp 243–246°. Recrystallization from chloroform (charcoal) gave white crystals, yield 2 g, mp 246–247°.

4-Amino-5-(quinolyl-6)-pyrimidine (VIII).—The dark, viscous reaction mixture was extracted with benzene for 24 hr. The benzene solution was treated with active carbon and the formed resin, on cooling, was separated by decantation. The solution was then concentrated, affording a crystalline product which dissolved in 10% hydrochloric acid. The solution was treated with active carbon and the product was precipitated by basification of the filtrate with 8% sodium hydroxide. The precipitate was crystallized from water, giving crude VIII as pale yellow crystals, yield 1.9 g, mp 163–171°. It was chromatographed on basic alumina by using 4:1 chloroform–benzene as eluent to yield a product, mp 186–193°. Recrystallizations from ligroin (bp 100–120°) gave white crystals of pure VIII, yield 0.4 g, mp 194–195°.

6-Quinolylacetamide.—In a flask with stopper, 21.5 g (0.1 mol) of 6-quinolylacetic ethyl ester[17] and 100 ml of ammonium hydroxide (27%) were shaken for 8 hr. The formed amide was separated and crystallized from alcohol as white crystals, yield 13 g (70%), mp 207–208°.

Anal. Calcd for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.05. Found: C, 70.71; H, 5.80; N, 15.10.

4-Amino-5-(quinolyl-8)-pyrimidine (IX).—The resinous reaction mixture was treated as in the case of II. The resin formed was removed and the alkaline solution was extracted with benzene for 24 hr to yield crude IX as pale yellow crystals, yield 0.8 g, mp 174–180°. Recrystallization from benzene (charcoal) gave white needles, yield 0.6 g, mp 186–187°.

4-Amino-5-methylpyrimidine (X).—The reaction mixture was treated with water, made alkaline with 8% sodium hydroxide, and extracted with benzene for 30 hr. Crude X was obtained from the benzene extract as pale yellow crystals, yield 0.2 g. Recrystallization from benzene (charcoal) gave white needles, yield 0.1 g, mp 178–179° (lit.[18] mp 175–176°).

4-Hydroxy-5-phenylpyrimidine (XI). A. Synthesis with Amide.—The reaction mixture was treated with a small amount of water and 8% sodium hydroxide and the unreacted amide was separated and regained after recrystallization, yield 22%. The alkaline filtrate was treated with active carbon, filtered, cooled, and saturated with carbon dioxide to pH 7–8 to precipitate XI, yield 0.9 g, mp 125–140°. The new filtrate was extracted with chloroform for 10 hr and the extract, after removal of chloroform and formamide [bp 95° (10 mm)], was dried on a plate, yield 1.8 g, mp 136–167°. The totally received crude XI was warmed on a steam bath with 10 ml of 36% hydrochloric acid for 1 hr to hydrolyze any unreacted amide. The residue, after evaporation, was dissolved in 8% sodium hydroxide and the solution was saturated with carbon dioxide to give XI, yield 1 g, mp 170–173°. Recrystallization from water gave white crystals, yield 0.8 g, mp 173–174° (lit.[4] mp 173–174°).

B. Synthesis with Ester.—The reaction mixture gave two layers. The upper layer, by distillation *in vacuo* [bp 120–121° (20 mm)], gave the unreacted ester, yield 50%. The lower layer was made alkaline with 8% sodium hydroxide, treated with active carbon, filtered, saturated with carbon dioxide, and extracted with chloroform for 10 hr. The hydroxypyrimidine XI was separated and purified as above. Recrystallization from water, after cooling in a refrigerator, gave white crystals, yield 0.03 g, mp 172–174°.

4-Hydroxy-5-α-naphthylpyrimidine (XII).—The unreacted amide was recovered in 45% yield as in procedure A for XI. The alkaline filtrate was treated with active carbon and saturated with carbon dioxide to precipitate XII, which was redissolved in 8% sodium hydroxide and reprecipitated with carbon dioxide. Recrystallization from benzene (charcoal) or alcohol gave white crystals, yield 0.6 g, mp 203–205°.

Attempted Reaction of I with α-Naphthylacetic Ethyl Ester.—In an analogous manner to procedure B for XI, no hydroxypyrimidine XII was obtained and the ethyl ester was recovered in 50% yield.

4-Hydroxy-5-(pyridyl-3)-pyrimidine (XIII).—The reaction mixture was allowed to stand overnight. The crystalline product was filtered,[19] dissolved in a small amount of 35% sodium hydroxide, and treated with active carbon. The filtrate was saturated with carbon dioxide and cooled overnight in a refrigerator, and the separated, crude XIII was crystallized from alcohol (charcoal) as pale yellow crystals, yield 3.3 g, mp 235–238°.

(10) A. Novelli, *Anales Assoc. Quim. Arg.*, **31**, 23 (1943).
(11) D. J. Brown, "The Pyrimidines," John Wiley & Sons, Inc., New York, N. Y., 1962, p 92.
(12) L. N. Short and H. W. Thompson, *J. Chem. Soc.*, 168 (1952).
(13) D. J. Brown and L. N. Short, *ibid.*, 331 (1953).
(14) J. A. Brownlie, *ibid.*, 3062 (1950).
(15) J. A. Montgomery, *J. Amer. Chem. Soc.*, **78**, 1928 (1956).
(16) H. Bredereck, R. Gompper, H. Rempfer, K. Klemm, and H. Keck, *Chem. Ber.*, **92**, 329 (1959).
(17) R. G. Jones, Q. F. Soper, O. K. Behrens, and J. W. Corse, *J. Amer. Chem. Soc.*, **70**, 2843 (1948).
(18) R. R. Williams, A. E. Ruehle, and J. Finkelstein, *ibid.*, **59**, 526 (1937).
(19) From the filtrate, after distillation of formamide and extraction of the residue with boiling chloroform, unreacted amide was recovered in 6% yield.

Recrystallization from alcohol gave white crystals, yield 2.2 g, mp 238–239°.

4-Hydroxy-5-(pyridyl-4)-pyrimidine (XIV).—In the same manner as above, crude XIV was obtained as pale yellow needles, yield 4.4 g, mp 280–283°. Recrystallizations from alcohol gave white needles, yield 3.5 g, mp 282–283°.

4-Hydroxy-5-*p*-nitrophenylpyrimidine (XV).—The reaction product was separated, dissolved in warm 8% sodium hydroxide, and treated with active carbon, and the filtrate after saturation with carbon dioxide, yielded XV as a yellow powder, yield 6 g, mp 330–332° dec. By redissolving the product in 8% sodium hydroxide and reprecipitation with carbon dioxide, pure XV was obtained as yellow needles, yield 4 g, mp 335–337° dec (lit.[2] mp 337° dec).

Attempted Reaction of I with Valeronitrile. Isolation of Bisformylaminomethane.—The reaction mixture was distilled to recover the unreacted nitrile in 71% yield. (The nitrile was purified from the distilled *s*-triazine by freezings and redistillations). The solid residue, after the distillation of formamide, was dissolved in water, made alkaline with sodium carbonate, and extracted with chloroform for 3 days to give a crystalline product, yield 0.5 g, mp 132–139°. Recrystallization from toluene (charcoal) gave white crystals of bisformylaminomethane, yield 0.3 g mp 140–141° (lit.[9] mp 142–143°).

Attempted Reaction of I with Caprylonitrile. Isolation of Bisformylaminomethane.—The reaction mixture gave two layers. The upper layer gave the unreacted nitrile, bp 205°. (The purification of the nitrile from *s*-triazine was obtained as previously.) The lower layer was made alkaline with 8% sodium hydroxide and the resultant oily layer of unreacted nitrile was removed (88% of the nitrile was totally recovered). The solution was then extracted with ether for 4 days to give a mixture of two layers. The upper layer was ether. The lower was distilled in vacuo to remove formamide, and the residue was treated with boiling methanol to yield a crystalline product, yield 1.4 g, mp 127–134°. Recrystallization from acetic ethyl ester (charcoal) gave white needles of bisformylaminomethane, yield 0.9 g, mp 140–141°.

4-Hydroxy-5-α-naphthylpyrimidine (XII) by Hydrolysis of II.—A solution of 11.1 g (0.05 mol) of II in 35 ml of 36% hydrochloric acid was heated on a steam bath in a stream of hydrogen chloride for 20 hr. The reaction mixture was made alkaline with 35% sodium hydroxide and the unreacted II was recovered in 18% yield by filtration. The filtrate was diluted with 50 ml of water and saturated with carbon dioxide to precipitate XII. Crystallization from water or alcohol gave white needles, yield 5 g, mp 204–205°. The yield of XII was increased to 56% when the hydrolysis time was 40 hr.

4-Hydroxy-5-(pyridyl-2)-pyrimidine (XVI) by Hydrolysis of III.—Compound III (8.6 g, 0.05 mol) was hydrolyzed as previously for 20 hr. The reaction mixture was evaporated on a steam bath under reduced pressure to remove the hydrogen chloride. The residue was dissolved in sodium hydroxide solution and extracted with benzene for 12 hr to remove unreacted III (0.5 g). The alkaline solution was then saturated with carbon dioxide and extracted with chloroform for 48 hr, yielding crude XVI. Recrystallization from acetic ethyl ester (charcoal) gave white crystals, yield 3.8 g, mp 181–183°.

4-Hydroxy-5-(pyridyl-3)-pyrimidine (XIII) by Hydrolysis of IV.—In the same manner as previously, crude XIII was obtained on the saturation of the alkaline solution with carbon dioxide, yield 4.1 g, mp 234–238°. An additional amount (1.5 g) of XIII was obtained by extraction of the filtrate with chloroform for 36 hr. Recrystallization from alcohol gave white crystals, yield 4.3 g, mp 238–239°.

4-Chloro-5-α-naphthylpyrimidine (XVII).—A mixture of 11.1 g (0.05 mol) of XII in 40 ml of freshly distilled phosphorus oxychloride was refluxed for 1 hr and then the excess of oxychloride was removed under reduced pressure. The residual resinous product was treated with ice–water and the crude XVII was separated as yellow powder. Crystallization from petroleum ether (bp 60–80°) with active carbon gave white crystals, yield 9.2 g, mp 99–100°.

4-Amino-5-α-naphthylpyrimidine (II) by Transformation of XVII.—A mixture of 0.5 g of XVII and 5 ml of alcohol saturated with ammonia gas was heated in a sealed tube for 4 hr at 150–160°. The alcohol was removed by evaporation under reduced pressure and the residue was extracted with boiling benzene to give, after recrystallization, II, yield 0.25 g, mp 195°.

4-Hydrazino-5-α-naphthylpyrimidine (XVIII).—To a slightly warm solution of 2.4 g (0.01 mol) of XVII in 50 ml of methanol, 10 ml of hydrazine hydrate was added and the solution was allowed to stand for 24 hr. Rhomboid crystals of XVIII were separated. Recrystallization from methanol (charcoal) gave white crystals, yield 1.9 g, mp 181–182°.

Registry No.—II, 22433-62-1; III, 22487-56-5; IV, 22433-63-2; V, 22433-65-4; VI, 22433-66-5; VII, 22433-67-6; VIII, 22487-57-6; IX, 22487-58-7; X, 22433-68-7. XI, 22433-69-8; XII, 22433-70-1; XIII, 22433-71-2; XIV, 22433-72-3; XV, 22433-73-4; XVI, 22433-74-5; XVII, 22487-59-8; XVIII, 22433-75-6; 6-quinolylacetamide, 22433-76-7.